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VOLUME LVI November, 1960 NUMBER 11

PERI-NATAL MORTALITY IN CHARLESTON, S. C.

HENRY HEINS, M. D.
Associate in Obstetrics and Gynecology,
Medical College of South Carolina
Charleston, S. C.

Because the dangers of childbirth have been reduced markedly in the last ten to twenty years, more attention is being directed toward fetal salvage. In 1957 in the U. S. fewer than 4 mothers in 10,000 did not live to raise their children. Better obstetrical care has reduced maternal mortality about 95 percent in the last two decades. Reductions in fetal and neonatal deaths have occurred simultaneously as an indirect dividend of this improved care.

This study covers the five year interval—January 1, 1954 through December 31, 1958, in three private white hospitals (Private Pavilion of Roper Hospital, St. Francis Xavier Hospital, and Baker Memorial Hospital) and the colored service at Roper Hospital.

Perinatal mortality has been used as an all-inclusive term for all fetal and neonatal deaths during pregnancy, delivery, and the postnatal period. Only relatively recently a somewhat stricter definition has been accepted. This is mortality among fetuses or infants that weigh over 1,000 grams at birth, who die before delivery or before the end of the first week postpartum. One can readily see that this definition, being stricter, will make comparable surveys possible. This definition is superior to those using gestational age in weeks or infant length.

Most authorities[1, 2] agree that infants of less than 1,000 grams seldom survive. This is due to immature development of the lung. After this weight is reached, the infant has adequate development to survive extrauterine life.

In the period covered, there occurred 20,562 deliveries which produced 189 infants weighing less than 1,000 grams. In this group of 20,373 deliveries there were 591 perinatal deaths. (Table 1).

HOSPITAL	NO. DELIVERIES 1954-1958	NO. DEATHS
OLD ROPER	8020	331
NEW ROPER	4940	98
ST. FRANCIS	5476	117
BAKER	1937	45
	20373	591

It soon became apparent that we were faced with two entirely different groups of patients—the private patient and the indigent patient. Similar studies[3-7] have reached the same conclusion that separation should be made.

There were 12,353 deliveries of infants weighing 1,000 grams or more with 260 deaths in the white patients group. There occurred 8,020 deliveries with 331 deaths in the colored group.

The perinatal mortality rate is computed as follows: (Table 2).

PERINATAL
MORTALITY RATE

NEONATAL DEATHS AND FETAL DEATHS
1000 GMS AND OVER X 1000

LIVE BIRTHS AND FETAL DEATHS
1000 GMS AND OVER

TABLE 2

Neonatal deaths and fetal deaths over 1,000 grams x 1,000. Live births and fetal deaths over 1,000 grams.

The perinatal mortality rate for each of the hospitals studied is given in Table 3. The difference in perinatal mortality in the various private hospitals is not statistically significant

PERINATAL MORTALITY RATE

OLD ROPER	=	40/1000
NEW ROPER	=	19/1000
ST. FRANCIS	=	21/1000
BAKER	=	23/1000

TABLE 3

as computed by the chi-square formula (Dr. Gavan of the Department of Anatomy, Medical College of S. C.). However, the difference between the colored group and private white group is highly significant. (Table 4).

COLORED (331)	WHITE (260)
40/1000	21/1000

TABLE 4

There is practically no difference in percentage of premature deaths (infants less than 2,500 grams) in both groups. One hundred and forty eight deaths (57%) were in premature infants in the private group, compared to 193 (58%) prematures in the indigent group (Table 5).

MATURE VERSUS PREMATURE
WHITE INFANTS ~ COLORED INFANTS

112 (43%)	MORE THAN 2500 GMS	138 (42%)
148 (57%)	LESS THAN 2500 GMS	193 (58%)

TABLE 5

An interesting finding was the difference in percentage of antepartum deaths (fetal and intrapartum) to neonatal deaths (Table 6). Sixty five percent (216) of the indigent deaths and forty seven (123) percent of the private deaths were still-borns. This higher figure is in keeping with the larger number of colored mothers being admitted with late pregnancy complications having been unattended or treated by a mid-wife.

NO ABNORMAL STATE
- WITH TOXEMIA
- WITH DIABETES
- WITH OTHER DISEASE
- WITHOUT MATERNAL DISEASE

INFECTION

HYALINE MEMBRANE DISEASE

OTHER CAUSES

CLASSIFICATIONS of PERINATAL DEATHS

ANOXIA
- ABRUPTION of PLACENTA
- PLACENTA PREVIA
- CORD
- PROLONGED LABOR
- OTHER (RUPTURED UTERUS)

MALFORMATIONS

ERYTHROBLASTOSIS

TRAUMATIC HEMORRHAGE
(BIRTH INJURY)

The causes of these deaths were determined by examination of the charts of the mother and infant and autopsy protocols. The classifications of death was similar to the one used by Nesbitt[8] and Potter.[1]

This classification includes eight broad

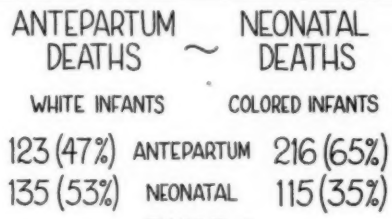


TABLE 6

groups:

1) Anoxia
2) Malformations
3) Blood dyscrasias (chiefly erythroblastosis)
4) Traumatic hemorrhage
5) No abnormal state
6) Infection
7) Abnormal pulmonary function (hyaline membrane)
8) Other causes

1. *Anoxia*

There are many causes of anoxia during pregnancy, labor and delivery but premature separation of the placenta is the most common (Table 7). There occurred 22 deaths due

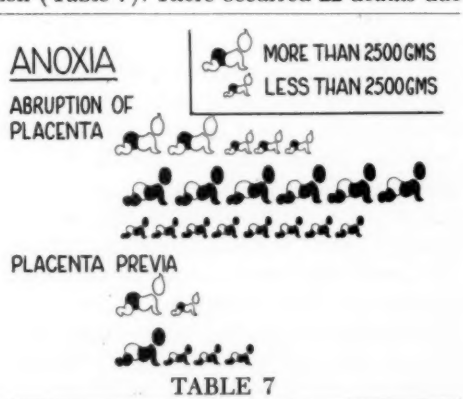


TABLE 7

to abruptio placentae in the private group while 62 deaths due to this same cause occurred in the colored group (8% versus 19%). This difference is no doubt due to the large number of toxemias admitted to the colored obstetrical ward. It was extremely interesting to note that five of the colored mothers were delivered abdominally with known dead fetuses due to the added complication of hypofibrogenemia with severe hemorrhage.

Placenta previa caused the death of 4 (1.5%) infants in the white group and 12 (4%) infants in the colored group. Prematurity was a very important factor in early delivery of these placenta previa infants as 14 of the total (16) were less than 2,500 grams.

The second most common cause of anoxia in this group of patients was prolapse of the umbilical cord (Table 8). This complication caused 18 deaths (7%) in the white group and 23 (7%) in the colored group of patients.

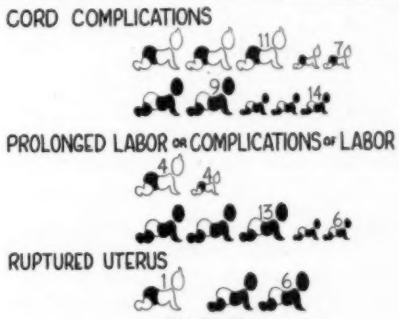


TABLE 8

Thirdly, prolonged labor or its complications was the next most important cause of deaths in the anoxia group. Eight infants (3%) died as a result of prolonged labor—one death in this group was an apparent direct result of intravenous pitocin stimulation with prolonged uterine contraction. This, however, was the only death in the entire group of 591 infants thought to be directly related to pitocin. Nineteen (6%) of the colored infants died as a result of prolonged labor.

Rupture of the uterus occurred once in the private group but occurred six times in the colored group.

2. *Malformations*

This group included only malformations which were incompatible with extra-uterine life (Table 9). There were 46 infants in this category of private patients (18%). In the colored group there were only 20 infants (6%). This increased rate of malformations in white private infants has been reported by others. There has been much experimental work in producing malformations in laboratory animals but little progress when actually ap-

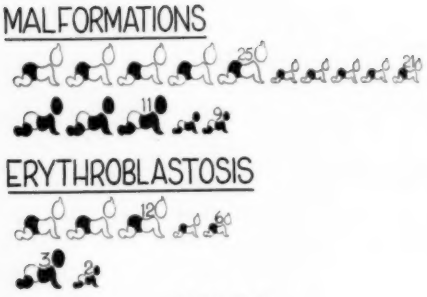


TABLE 9

plied to humans. We are all familiar with viruses as etiological agents for some malformations, particularly since the attention given to German measles. But there is little likelihood of damage to the embryo if the disease occurs after ten weeks of gestation.

There are many other causes of congenital malformations. Genetic defects inherited from the parents no doubt play an important role. Also to be considered are environmental factors within the genital tract of the mother. Attention is now being focused also on irradiation as an increasing factor in producing these defects. Lastly, the use of androgenic and progestational steroids have been incriminated by some investigators as causing varying degrees of virilization of the external genitalia of the female newborn.

3. *Blood Dyscrasias*

By far the most important group of infants in this category were the erythroblastotic deaths. There were 18 (7%) infants in the white group and only 5 (1.5%) in the colored group. This is in keeping with the higher incidence of Rh negative mothers in the white race.

The frequency of fetal deaths from erythroblastosis among immunized women has shown no reduction and there is no way known at present by which these deaths can be prevented. The frequency of a fatal outcome in a live born non-hydropic infant has been reduced recently since it has been recognized that a high blood bilirubin is the damaging agent and that this can be prevented by good pediatric care beginning at birth. Potter has estimated that the woman who has had one or more fetal deaths from erythroblastosis has no more than a 10-20% chance of having a surviving child in the next pregnancy. The premature induction of labor if the cervix is ripe at 37-38 weeks or cesarean section should be considered if the husband is homozygous and there is a rising antibody titre. However, we have to avoid compounding the confusion by not terminating the pregnancy so early as to end up with a weak premature infant which will be a challenge to the pediatrician.

4. *Traumatic Hemorrhage*

This grouping of patients included spontaneous deliveries as well as difficult operative deliveries (Table 10)—all in fetuses with

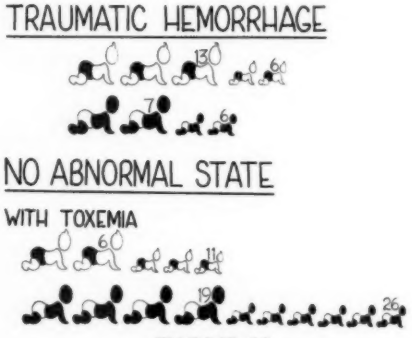


TABLE 10

intracranial or other types of traumatic hemorrhage. In the white group there were 19 (7%) neonatal deaths resulting from birth injury. There occurred only 13 (4%) such deaths in the colored group. In going through the data one gets the impression that more difficult forceps application occurred in the private group. There appeared more frequently also in the private group evidence of too early intervention or attempt at delivery without adequate pelvimetry studies.

The patient who has a contracted pelvis or a large baby can be allowed an intelligent test of labor and if good progress fails to occur abdominal delivery can be done safely. There is no place in modern obstetrics for the application of forceps on the unengaged head. Version and extraction has about completely disappeared except for delivery of the second twin.

5. *No Abnormal State*

As previously mentioned this category of

infants showed no abnormal state on examination but were divided into four groups:

1. With toxemia,
2. With diabetes,
3. With other diseases such as pyelonephritis, infectious hepatitis, perforated appendix, etc.,
4. Without maternal disease.

This broad group was largest of the eight in both the white and colored patients making up 103 (39%) in the white and 124 (37%) in the colored.

The "with toxemia" group was much larger in the colored patients, 45 or 13.5% to 17 or 6.5% as one would expect. There is a much higher percentage of toxemic patients delivered in the colored division of Roper Hospital. Thirty seven of the 45 colored infants lost in this group were fetal deaths. This demonstrates the importance of timing the induction of labor in severely toxic patients. One has to decide which is safer for the infant, intrauterine or extrauterine existence.

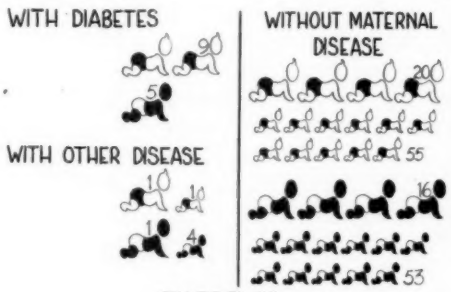


TABLE 11

The "with diabetes" group showed little difference, 9 fetal deaths (3%) in the private patients and 5 fetal deaths (1.5%) in the colored group. The trend recently has been to induce labor if the cervix were favorable at 38 weeks gestation. If the cervix were not favorable abdominal delivery was advised to avoid fetal death in utero during the last two weeks of pregnancy. (Table 11)

The "with other disease" group was made up chiefly of infants whose mothers had renal disease. Pyelonephritis was the most common type.

The fourth and most important group of infants without abnormal state were infants born of mothers without maternal disease. This is the largest single group in the series. These are the patients who succumbed for no obvious reason. One hundred and eight of the patients (55 white and 53 colored) had spontaneous onset of premature labor with loss of the premature infant. The etiology of this premature labor is obscure as is the cause of the onset of term labor. The incidence of premature delivery is higher in the colored group as has been reported in other indigent groups. Eight to nine percent of deliveries in colored patients in Roper Hospital were infants of less than 2,500 grams. The percentage of premature deliveries in private practice is nearer six per cent. In many instances efforts were made to stop premature labor with large doses of opiates. Here the difficulty was compounded by delivery of a narcotized premature infant. It has been emphasized that more prematures could be salvaged by the avoidance of analgesics than by any one pediatric measure.

6. *Infection*

Intrauterine infection of the fetus most commonly takes the form of pneumonia and is almost always caused by bacteria in the amniotic fluid which is aspirated by the fetus. Six infants (2.3%) in the white group died because of pulmonary infections primarily. Twenty five infants (6%) in the colored group were lost because of this same reason (Table 12). Pro-

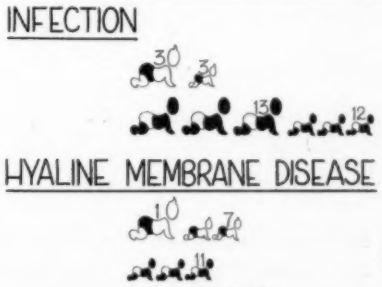


TABLE 12

longed or desultory labor may produce hypoxia in the fetus and increase the likelihood of aspiration of amniotic fluid. After premature rupture of membranes antibiotic therapy throughout the latent period does nothing to prevent intra-partum infection, nor does it

have a beneficial effect upon reducing perinatal mortality. It is the usual policy to give antibiotic therapy intensively during labor and the puerperium. Infective lesions which cause death within the first three or four days after birth have usually been contracted intrapartum. Infants more than a few days old may meet for the first time with infections from other sources than the mother.

An infection relatively mild in a mature infant may be fatal to one which is premature. Premature infants are very susceptible to respiratory tract infections.

Hyaline Membrane

This diagnosis was made in 8 (3%) white infants and in 11 (3%) colored infants. The etiology of this syndrome is obscure but the two most popular theories are:

1). The hyaline material is a transudate from the blood vessels in the alveoli.

2.) This material is aspirated amniotic fluid.

The incidence is thought to have lessened since the use of lessened oxygen concentration in premature incubators. The use of a sodium bicarbonate solution intravenously has recently been reported as helpful in this condition.

Table 13 shows the autopsy percentage in each of the hospitals studied. Sixty eight percent of the colored deaths were studied post partum. This higher figure is due to follow up by the house-staff. The lower percentages in each of the private hospitals need to be improved.

AUTOPSY PERCENTAGE

COLORED ROPER	[331]	225 = 68%
WHITE ROPER	[98]	56 = 57%
ST. FRANCIS	[117]	32 = 27%
BAKER	[45]	15 = 33%
TOTAL	[591]	328 = 56%

TABLE 13

Autopsies must continue to be energetically sought so as to expose the ultimate conditions responsible for death. Most parents are willing to grant autopsy permission when the importance of the procedure is explained to them. We cannot expect our Pathology Department to cooperate if we send sketchy or no clinical information with the request for autopsy. For complete value of the postmortem examination all significant clinical facts should be recorded on the chart. Most Pathology Departments are overburdened and do not receive official credit for examination of newborns but cooperate when requested to help with the diagnosis. This, however, does not mean the routine request for examination of the 500 gram macerated stillborn infant. Routine requests for autopsies on this type of material rapidly produces a deterioration of interest on the part of the pathologist, particularly when no information is available and no one exhibits any clinical concern.

In 1958 a coordinated program with the Charleston County Health Department was begun in an effort to encourage earlier registration at prenatal clinics and encourage postpartum follow up examinations. The Public Health Nurses made daily rounds on the obstetrical wards discussing the problems of the patients. They held conferences in the clinic discussing conception, growth of the fetus, labor, child spacing and sibling rivalry. This program, plus the moving of the indigent patients to the Medical College Hospital, certainly should have some beneficial effect. It is planned to repeat this perinatal death study in the next five year period, 1959 through 1963.

During the five year interval of this study (1954-1958) fifteen mothers died in Charleston County. Thirteen of these mothers were colored and two were white (Table 14).

MATERNAL MORTALITY 1954-1958
15 MOTHERS DIED

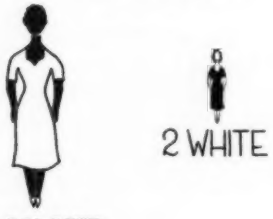


TABLE 14

Why the tremendous difference, both in perinatal mortality and maternal mortality between the colored and white patient? We glibly theorize about socio-economic factors such as diet, lack of education, substandard living, etc. (Table 15). Obviously these colored patients are not receiving prenatal care and therefore get inadequate care. The physical facilities are present in the form of County Clinics and the Medical College Out-Patient Clinic. A recent study (Keummerer) showed that in 1958 less than 5% of the clinic maternity patients registered by the fourth month of gestation. The majority registered by the sixth or seventh month. These people have to be informed that care is available and should be taught to register early in pregnancy.

How important is the emotional factor? Approximately one third of these colored deaths were in illegitimate infants. This is in keeping with the rate of 32% illegitimacy in the colored birth statistics for 1958 compared with 4% for the white race in Charleston County. This means approximately one out of every three Negro children does not have a stable home. He will not have the proper food, clothes, schooling, moral training and emotional security he needs. He will be a drain on the taxpayer from a health, education, delinquency and crime standpoint.

This study does not include those aftermaths of the reproductive failure problem such as cerebral palsy, epilepsy and mental retardation. Other areas of this problem were not studied such as: preventability, ratio of patients delivered by general men or specialists or the number of infants that died after seven days of life.

Summary and Conclusion

1). The perinatal deaths for the past five years in three private hospitals and one indigent service have been studied.

2). The causes of perinatal mortality need to be identified because they must also be the causes of congenital handicaps in infants who do not die.

3). The perinatal mortality rate is much higher in the indigent group as is maternal mortality and number of premature births.

4). It is believed that a reduction in perinatal mortality can occur with increased dissemination of knowledge of perinatal care to the indigent group of patients.

5). It is recommended that a code sheet be attached to every perinatal death chart so that the attending physician can record details of the patient's care while these details are fresh in his mind. All of us forget! ! ! !

The author acknowledges with thanks the assistance toward publication by The Division of Maternal and Child Health of the S. C. State Board of Health.

REFERENCES

1. Potter, E. L.: Planning perinatal mortality studies. Obst. & Gynec. 12:243, 1959.
2. Baumgartner, L. and Pakter, J.: Challenge of fetal loss, prematurity, and infant mortality—assessing the local situation. J.A.M.A. 167:936, 1958.
3. Nesbitt, R. E. L., Jr.: Perinatal Loss in Modern Obstetrics. Philadelphia, F. A. Davis, 1957.
4. Flowers, C. E., Jr., Weinel, W. H., and Kirkland, J. A.: Perinatal mortality in the North Carolina Memorial Hospital, 1952-1958. J.A.M.A. 169:1037, 1959.
5. Verhoestraete, L. J. and Puffer, R. R.: Challenge of fetal loss, prematurity, and infant mortality—a world view. J.A.M.A. 167:950, 1958.
6. Eliot, M. M.: Deaths around birth—the national score. J.A.M.A. 167:945, 1958.
7. Diddle, A. W., DeLozier, O., O'Connor, K. A., and Lambeth, S.: Perinatal mortality in three general hospitals. Obst. & Gynec. 8:323, 1956.

GRISEOFULVIN AND PING PONG MYCOSIS—MONILIASIS

JOHN VAN DE ERVE, M. D.
Clinical Professor of Dermatology,
Medical College of South Carolina
Charleston, S. C.

The advent of an antibiotic effective against fungi is comparable to the appearance of penicillin some years ago. Griseofulvin is a welcome addition to our treatment of fungous diseases. But, like penicillin and the sulfonamide drugs, it has dangers and drawbacks, and it is not an unmixed blessing.

What is it? It is the fermentation product of Penicillium griseofulvum, patulum, and janczewski. Penicillin comes from Penicillium notatum. But, perhaps because griseofulvin does not contain nitrogen, cross-reactions have not been reported and it has been used safely in several penicillin-sensitive patients. It was discovered in 1939 and, like penicillin, was laid aside and forgotten. In 1946, practically rediscovered, it was used widely as an agricultural fungicide on lettuce and tomatoes. In 1958 Gentles reported on its experimental use in guinea pigs and there the "anti-serendipity" finally ended and human trial showed marked value for fungous infections of the skin, hair, and nails.

How does it act? It is a "single-minded" narrow spectrum antibiotic, acting only on trichophyton, microsporum and epidermophyton fungi which ordinarily grow in the keratin layers of the skin. We must remember that the skin is constantly growing outward, the effluvium of the keratin-horn cells being steadily cast off. The fungous infection has to grow and penetrate inward faster than the keratin grows outward. Griseofulvin is absorbed from the gastrointestinal tract and is deposited in concentration in the keratin of skin, hair, and nails sufficiently to be fungistatic. It produces gross distortion, thickening and curling of the hyphae. Cure is complete only when the viable but inactive fungi are gradually exfoliated and replaced by uninfected tissue.

Since it is able to inactivate only the superficial fungi of the skin, hair, and nails, it does not help deep fungous infections. It also tends to produce secondary yeast or monilial infections just like other antibiotics and has no effect on the growth of monilia (candida).

Since it comes from one of the penicillium molds, the question of cross-sensitization and danger of use in patients highly sensitive to regular penicillin was considered. So far, experimental use in a number of penicillin-sensitive patients has not produced any reactions. Penicillinase, specific for penicillin, does not have any effect on griseofulvin in the body. It is therefore probably as safe as any other drug in penicillin-sensitive patients.

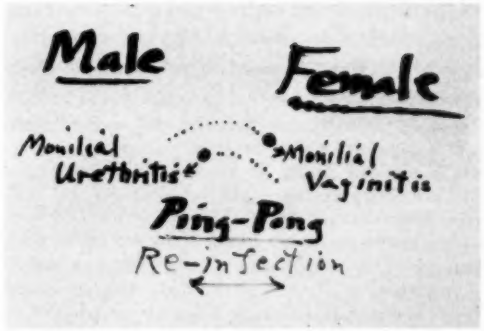
Indications: Griseofulvin does not affect the growth of bacteria and yeasts or monilia (candida albicans). It also does not affect superficial tinea versicolor (probably because this group of fungi do not penetrate deeply enough to enter the zone where new keratin is formed). Apparently the presence of fungi in

the skin inhibits the growth of monilia. Also, monilia and fungi may coexist as a double infection with the monilium as underdog and subclinical in activity until the balance of inhibition is lifted by removal of fungal depression by treatment of various kinds, after which monilia may grow in great profusion, unhindered by adverse circumstances. Monilia do not have much "get up and go" and are easily discouraged, but when conditions are ideal, they cause much inflammation and trouble. Monilia are often present without symptoms in the vagina and sometimes in the urethra of the male, which leads to marital ping-ponging of infection. Recent work has also demonstrated that in many families where one person has T. rubrum fungous infection, small patches of fungus may be demonstrated in up to 60% of the rest of the family groups. (Recent work in India by DeSai).

Since griseofulvin is so efficacious in simple fungous infections, the diagnosis must be established by an examination of the scrapings, softened by warmed 20% potassium hydroxide, under the microscope, and if at all possible, by culture on Sabouraud's medium. On this medium both fungi and monilia grow well and the presence of one or both may easily be demonstrated. Incubation is not necessary. Small perfume bottle culture media can be purchased cheaply at surgical supply houses for this purpose. (In my office, we make up 500 of these at a time and discard the bottle when the culture has been finished). All one needs to do is to scrape the infected skin onto a slide for immediate examination and into the culture vial for later identification.

The importance of knowing the diagnosis is illustrated by the fact that local treatment is always necessary, even during the period of administration of the antibiotic. Also, the treatment must take care of both fungi and yeasts, if necessary, and sometimes a bacterial infection. This is particularly true of acute vesicular eruptions of the feet which respond ordinarily to old-fashioned local treatment and the use of expensive griseofulvin is not justified.

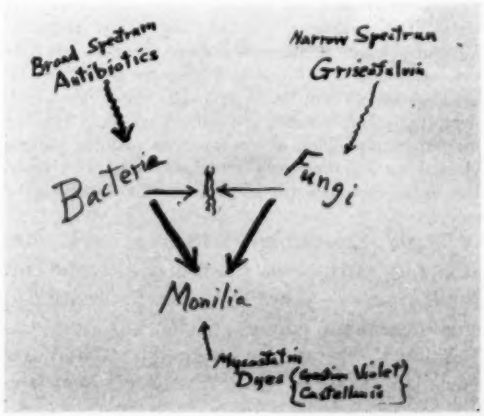
To have a clinical diagnosis completely established, one must find hyphae (the growing active phase of the fungus); the growth



must be in the deeper layer of the skin where new keratin is formed; moisture for growth must be present; and there must be some keratin defect or faulty immunity which allows the fungus to grow in the patient's skin. Under these circumstances, griseofulvin is justified and, unless there is intolerance, it should be given. The optimum dose is still four tablets of 250 mg. or one gram daily. Less than this increases failures. Resistance so far has not been reported.

Contraindications: Urticaria, erythema multiforme, generalized erythrodermia have been reported, sometimes very severe. Headache and nausea can usually be controlled while continuing the drug. A blood count and urinalysis should be done before instituting treatment and should be repeated twice monthly as indicated. So far, there is no cross-sensitivity with penicillin.

Monilial flareup in the griseofulvin-penetrated skin is becoming more common and



often results in an acute wet dermatitis. Ping-pong reinfection of each infection may continue for a long time. Several illustrative cases follow.

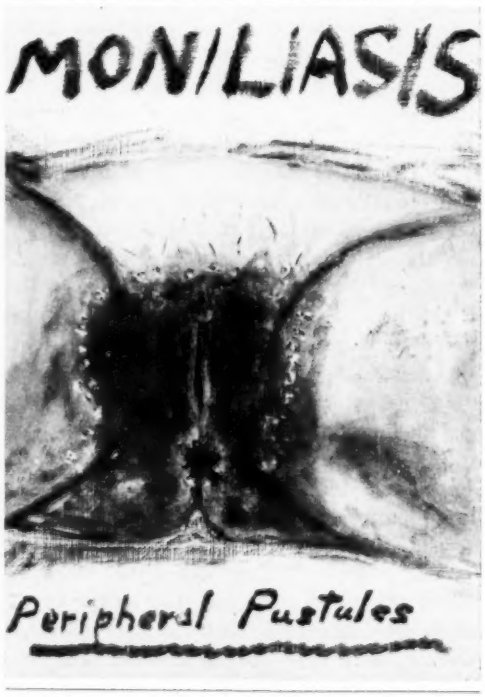
CASE 1. Adult male 60 years old, with dry skin and a crural dry scaling eruption was given griseofulvin in adequate dosage for one month. He then began to have severe itching, acute wet erythema and vesicles, with scattered border pustules in the periphery of the pubic and thigh areas. This then produced a general scaly erythematovesicular autosensitization dermatitis over the rest of the body which required heavy corticosteroid therapy to control, in addition to local treatment of the skin to resolve the monilial infection which was proved by culturing the skin. In this instance there were several flareups, one of which showed fungi again and required carbol-fuchsin paint to control. The senile dry skin required a good deal of followup care before the eruption subsided.

CASE 2: Boy, 16, developed crural dermatitis which showed fungi in scrapings and on culture. He was given griseofulvin and local fungicides and was almost clear three weeks later when he began to have acute redness and vesicular eruption of the crurae, thighs, and extension of dermatitis on to the scrotum (this area is almost always immune to mycotic invasion in ordinary cases). Culture showed a heavy growth of monilia and treatment with mycostatin ointments rapidly cleared it up. Treatment was discontinued but the monilial infection flared up several times and treatment with monilicides was necessary for three weeks more.

CASE 3: Male, married, age 35. In fall of 1959 he developed an acute erythema of the crural areas and was given griseofulvin for a month. The condition improved temporarily, then flared acutely with vesicopustules, and involvement of the scrotum. Fungicidal treatment made this worse. Cultures later showed monilia and on treatment with mycostatin lotions, the condition cleared up. Several weeks later the condition recurred, and scrapings showed hyphae of fungus infection but treatment for this made him worse. Recurrent attacks continued for two months, during which time he cleared up at intervals. Patch tests to medications and clothing were negative. Several cultures at intervals showed monilia. His wife was examined and found to harbor an asymptomatic monilial infection of the vagina. She was treated with mycostatin suppositories and with douches to stop the marital ping-ponging of the infection and the patient cleared up and has since remained clear. The problem is much more troublesome in the female as a rule.

Recent Experience: Within a week after stopping griseofulvin, fungi may often be cultured from the skin. This calls for continued treatment long enough to be sure that the fungi in the keratin, even though stunted and curled up, can be entirely cast off from the skin. This may be achieved more rapidly by local treatment with mild peeling standard fungicidal topical agents.

2. Fungous infections of the scalp show the same stunting in the hairshafts and the hairs should be shaved from the scalp every week, carefully putting the clippings into paper and burning them. The purpose of this is to avoid reinfection from the patient's own hairs. Average treatment is one gram a day for eight weeks. Single dose methods are not quite as



good. However, repeat infections seem, so far, to respond to a second course of griseofulvin as well as in the beginning. Resistance, so far, is not a problem.

3. On smooth skin treatment for four weeks is usually sufficient, especially if mild peeling locally with resorcin and salicylic acid, in cream or lotion, is also used to rid the keratin of the frustrated fungi.

4. Fingernails grow much more rapidly than toenails. Thus a course of three or four months may take care of fingernail mycosis where seven months may be necessary for toenails. Some surgeons are now avulsing the nails

while giving griseofulvin. Results are good but this is a rather heroic and unnecessary extension of treatment. The nails may be continually scraped down (in the office with electric dental bur) at home with a sharp-edged piece of glass (microscope slide or go out in back yard and bust a bottle on a rock.) Dr. O'Leary of Mayo Clinic always suggested pieces of broken light bulb, the glass being thin enough to break easily and not cut so severely, while at the same time being firm enough for scraping.

5. Acute Foot Dermatitis is as often a contact, sweating maceration, other infection, etc. as it is a fungous infection and local treatment is still the best. Chronic, dry, mycotic infection of the feet (negative patch test for shoe dye sensitivity and positive culture for fungus) does justify the use of griseofulvin.

6. Superficial tinea versicolor macules on the chest do not penetrate deeply enough into the new keratin-forming layer and are therefore not improved by griseofulvin treatment. Local use of griseofulvin ointment is now being tried(previous use was not found very helpful) to see if enough penetration of the superficial layer may be achieved. The problem of resistent and persistent spores is the chief trouble here.

7. One must keep in mind the fact that Tinea tonsurans has, in the past few years, come up from "South of the Border" to cause ringworm of *adult* scalps. In very persistent, chronic seborrheic dermatitis, it may pay to culture the hairs (there is no fluorescence under black light with this fungus) and if the infection is present, give griseofulvin. This was a very resistent infection to older methods of treatment.

8. There is apparently no effect on spermatogenesis. This has been thoroughly studied in adult males. Studies have not been completed on prepuberty stage but indications are that the drug, in the dosages now being given, is quite safe. Spermatogenic effects in rats were due only to relatively enormous dosage.

Summary:

1. Be sure of the diagnosis by doing microscopic examination and culturing the tissue.

2. If monilial infection is present, treat it first with mycostatin, dyes, wet dressings and carbol-fuchsin paint. Unwise administration, "in the dark", with griseofulvin may cause acute general flareup and severe dermatitis. This is most dangerous in hot weather.

3. Help the systemic treatment along by mild exfoliation and peeling off the infected skin, nail, or hair to get rid of stultified but still viable fungus in the keratin layers.

4. Griseofulvin, while not the panacea hoped for, is still one of the most valuable antibiotics to appear since penicillin and should be used with masterful reasonableness whenever it is definitely indicated in the control of fungous infections.

THE INCOMPETENT INTERNAL CERVICAL OS:

A Review of the Current Literature

JOHN J. ZADWORNY, M. D.
Dept. Obstetrics and Gynecology,
Columbia Hospital,
Columbia, S. C.

The etiology of abortion lies anywhere within the conditions needed to be fulfilled for a conception to reach maturity. Most conceptions result in a normal infant, however some women are not so fortunate. To them, an abortion is a serious and depressing affair. What can be done for this woman? Over the years the problem of abortion has been of foremost interest in the minds of obstetricians and gynecologists. Because of such interest and investigation a relatively new etiologic syndrome has been advanced, that of the incompetent internal cervical os. This is characterized clinically by the story of a woman with multiple pregnancies, a very few of which come to term or even produce a premature viable child. In the late second or early third trimester there is a sudden rupture of the membranes followed by a rapid and relatively painless extrusion of the products of conception.

Aschoff in 1906 demonstrated the intimate anatomy of the uterus and cervix, showing that the upper part of the cervical canal and the anatomical internal os were incorporated into the lower segment of the uterus at an early stage of pregnancy. However, between the anatomical internal os and the lower uterine segment is a fibromuscular junction and it is this area that plays the important role of maintaining the pregnancy in utero. When the isthmus begins to unfold in the late second and third trimester of pregnancy, it is this accumulation of cervical muscle which acts as a compressor and prevents premature herniation of the membranes. In a careful anatomical study the precocious movement of this circular layer of muscle in a case of habitual abortion was observed by Hughesdon.[5]

How is this condition diagnosed? The history is the most important clue. A history of repeated pregnancies and their untimely loss near viability, especially with the factor of premature rupture of the membranes is most suspicious. Usually these women conceive easily and generally carry the pregnancy uneventfully until the latter part of the second trimester. At this time there is a sudden unexplained rupture of the membranes followed by premature labor and loss of the fetus. This recurs repeatedly in the same woman, usually in the same way. What has happened is that the fibromuscular junction has been unable to retain the growing conceptus, the membranes have herniated through a partially opened cervix which has painlessly and progressively effaced itself and dilated. This occurs in the absence of uterine contractions, bloody discharge or discomfort. One can see these insidious changes taking place in the cervix by examining these patients at weekly intervals starting after the 14th week.

There are other methods of diagnosis. With an anatomical defect in the region of the internal os, Palmer[9] states that an 8 mm. Hegar dilator should traverse the internal os in the non-pregnant uterus without resistance. Durfee[3] prefers to use an olive tip sound. If there is a failure of the integrity of the internal os the olive tip of the sound moves in and out of the uterine cavity with great ease. This is not true of the normal state in which the sound passes into the uterus with difficulty and is removed with even greater difficulty because the tip hangs up at the level of the internal os. Interestingly, such instrumentation of the cervix with this defect causes almost no pain to the patient.

According to Lash and Lash[6] the pathology may be palpated most easily following an abortion. With the finger in the cervical canal a defect in the form of a thin scar can be pal-

pated. This is usually anterior in the Lashs' experience. With the bladder dissected off the cervix, the thin scar is especially evident with the defect varying from 1 to 2 cm. in width and 2 to 3 cm. in length. There are two radiographic methods to demonstrate the defect.[11] In the first technique, a balloon is inserted into the uterus over a Best-Mixter canula and with traction on the balloon the cervico-uterine angle and its integrity is outlined. The second method is that which utilizes a Rubin canula and lipiodal. In the normal uterus, the Rubin canula tip completely fills the internal os and there is no flow of lipiodal into the cervical canal around the canula tip. In the presence of an incompetent cervical os the reverse is true. When the canula tip is removed another picture will demonstrate any widening of the internal os as the lipiodol runs out of the uterus.

The etiology of the incompetent internal os is usually associated with trauma: a curettage with too much zeal; a dilatation (probably over dilatation with resulting laceration); previous abortion followed by curettage; vaginal hysterotomy; precipitate labors; lower cesarean section; Duhrssens' incisions. According to Heaney "the greatest contributing factors, in my experience to this condition are tearing of the cervix by labor or by instrumental dilatation . . . ." The frequency with which the incompetent cervix is encountered is estimated to be 3 times per 1000 deliveries.

Initial efforts at surgical repair of this condition were first done as early as 1941. The first reported repair in the American literature was in 1950 by Lash *et al.*[6] This first technique was a simple pleating of the thinned out portion of the cervix at the level of the internal os where the defect was noted, performed immediately after abortion. The next type of repair included the removal of an elliptical segment of cervical tissue without destroying the continuity of the external os after which reconstruction of the cervical canal was accomplished. At present Lash utilizes a wide resection of the upper middle third of the cervix, extending into the lower uterine segment, which is then closed by a double layer of sutures.

All of these processes produce scarring of the area, which is the background of the hope for prevention of relaxation and dilatation of the cervix. Suture material has ranged from kangaroo tendon or catgut to fine tantalum wire. The repair is now carried out 3 to 4 months following the abortion. Baden[1] has utilized the principle of trachelorrhaphy during pregnancy with good success.

In 1954 at the International Congress on Obstetrics and Gynecology in Geneva, Shirodkar[13] proposed a new repair. His reasoning was that the defect in the internal os was more frequently in positions other than the anterior cervix and thus a more logical repair would be a method of encirclement by means of a fascial strip forming a pursestring around the internal os. The great advantage of this procedure is that it can be accomplished during pregnancy and that it preserves pregnancy without endangering the patient's fertility. The fascia used as described by Shirodkar was that of the patient's fascia lata. The fascia, 1.5 cm. wide by 10 cm. long, is inserted beneath the vaginal mucosa at the region of the internal os by means of the following technique:

> Under general or regional anesthesia with the patient in Trendelenberg position the anterior lip is grasped with a sponge forcep. A transverse incision is made in the vaginal-cervical junction and the submucosa and bladder are pushed upwards to expose the region of the histological internal os, which lies about 1½ inches above the external os. The posterior lip is now grasped and a small vertical incision is made at the same site on the posterior surface of the cervix. The submucosa is bluntly deviated to the right and left and then by means of special instruments such as large aneurysmal needles or Gallie fascial needles, the fascia is guided into place and is sutured at the level of the internal os. The fascia is then tied and is anchored anteriorly and posteriorly by means of catgut sutures.

Since Shirodkars' publication many modifications of this technique have been introduced. Durfee[8] now uses prepared ox fascia and ties the ox fascia anteriorly before anchoring the fascia in place. The objection to the use of ox fascia is that many people cannot tolerate this material, with a resultant sloughing of the fascia. In other cases failure has been reported due to complete absorption of the fascia with the loss of the fascia and consequent loss of the strengthening purse string. Page[8] has further modified this procedure in

that he uses four strips of fascia. The mid-portion of each fascial strip is anchored at 3, 6, 9, and 12 o'clock and the ends are tied with the knots placed at 2, 5, 8 and 11 o'clock. In addition the area is sprinkled with talcum powder in order to increase granulation and strengthen the scarring. More recently the fascia has been replaced with synthetic fibers such as Mersiline, a synthetic dacron material originally designed for vascular grafts, and Permofil, a new inert protein non-allergenic material. At present Shirodkar has abandoned the use of fascia and uses a 3 mm. wide nylon tape and has experimented with kangaroo tendon. Green-Armytage and Brown[4] prefer to use 7N or 8N nylon, tying the knot posteriorly in order to avoid irritation to the bladder. If need be, they have used a second or third nylon ligature, using as many as required to close the endocervical canal.

Most authors agree that the ideal time for the surgical repair is about the 18th or 22nd week of gestation. The procedure is not recommended in the first trimester because of the risk of abortion from other causes. Before undertaking the procedure it is felt that the patient should be examined at weekly intervals and effacement and dilatation confirmed to be occurring insiduously. Certainly the diagnosis of incompetency should never be made on the basis of a single examination. Riva[11] has performed the operation twice on the same patient during the same gestation, the second operation necessitated by a sloughing of the fascia shortly after the initial repair.

Considering Malpas[7] statement that after 3 abortions the chance of carrying a pregnancy to term was 27 per cent, the results of the operation are very encouraging. Riva when he first presented his figures in 1956, had raised the fetal salvage from 17.4% to 45.4% in his first group of patients. Since then in his series of 50 patients, 40 have been successfully delivered of a viable baby. In 1957 Green-Armytage and Browne[4] report 100% success in 7 patients. Durfee[3] reports a fetal salvage of 70% in a group of 24 women whose previous salvage rate was 20%.

The majority of operators advise delivery by cesarian section. Those utilizing ox fascia have permitted the patient to deliver vaginally but keeping in mind the occasional necessity of cutting the fascia to prevent uterine rupture. Once the fascia has been cut the cervix is again rendered incompetent and in all likeliness, a repair will be required with the next pregnancy. The authors using Mersiline vary in their methods of delivery. About one half prefer to deliver their patients by section and the others cut the Mersiline gauze at time of labor.

Reduction of premature infant mortality and morbidity is one of the goals most sought after in modern obstetrics. Support of the incompetent cervix offers great hope in reducing fetal wastage by preventing the birth of a near viable child. However unless rigid criteria are established as to the indication for cervical re-enforcement and great care exercised in the selection of patients, it is easily possible that the hoped for reward of a viable infant may result in abuse of a sound procedure.

It must be repeated again and again that the number of patients who have true incompetence of the cervix is extremely limited. The operation is of benefit to only a very few patients. It is no panacea except for a very specific type of abortion. In these select patients, it affords the woman a promising method to restore her natural childbearing function.

REFERENCES

1. Baden, W. F. and Baden, E. E.: Cervical incompetence; repair during pregnancy. Am. J. Obst. & Gynec. 74:241, 1957.
2. Barter, R. H.: Operations to preserve pregnancy. Clin. Obst. & Gynec. 1:963, 1958.
3. Durfee, R. B.: Surgical treatment of the incompetent cervix during pregnancy. Obst. & Gynec. 12:91, 1958.
4. Greene-Armytage, V. B. and Browne, J. C. M.: Habitual abortion due to insufficiency of the internal cervical os. Brit. M. J. 2:128, 1957.
5. Hughesdon, P. E.: The fibromuscular structure of the cervix. J. Obst. & Gynaec. Brit. Emp. 59:763, 1952.
6. Lash, A. F. and Lash, S. R.: Habitual abortion: the incompetent internal os of the cervix. Am. J. Obst. & Gynec. 59:68, 1950.
7. Malpas, P.: A study of abortion sequences. J. Obst. & Gynaec. Brit. Emp. 45:932, 1938.
8. Page, E. W.: Incompetent internal os of the cervix causing late abortion and premature labor; technic for surgical repair. Obst. & Gynec. 12:509, 1958.
9. Palmer, R.: Le role de la beance de l'isthme uterin dans l'avortement habituel. Rev. franc. gynec. et obst. 45:218, 1950.
10. Picot, H., Thompson, H. G. and Murphy, C. J., Jr.: Surgical treatment of the incompetent cervix

in pregnancy. Obst. & Gynec. 12:269, 1958.
11. Riva, H.: Personal communication, 1956.
12. Rubovits, F. E., Cooperman, N. R., and Lash, A. F.: Habitual abortion: a radiographic technique to demonstrate the incompetent internal os of the cervix. Am. J. Obst. & Gynec. 66:269, 1953.
13. Shirodkar, V. N.: A new method of operative treatment for habitual abortion in the second trimester of pregnancy. Antiseptic. 52:229, 1955.

Somatopsychic Disorders. Vince Moseley (Charleston) Tri-State M. J. V. 8; 6-10 (May, 1960)

Although students of psychosomatic disease have contributed much towards a better appreciation and understanding of the unity of relationships between soma, psyche, and spiritual factors, practicing physicians must be continually aware that patients may present dominant psychiatric or emotional manifestations as a result of disturbances of internal homeostatic mechanisms, and when due to a curable disease, the primary management is medical. Local lesions effecting the central nervous system of various etiology, endocrine disturbances and renal or hepatic disease may be initially manifested as derangements in emotional or psychic areas.

The energy requirements for cerebral or nervous function are chiefly derived from glucose oxidation, any disturbance relating to glucose concentrations or factors which interfere with substrate oxidation produce mild to severe impairment in cerebral function and, in severer degree, anatomical injury or death. Disturbances in tissue oxidation resulting from such factors as iron deficiency or anemia are frequently accompanied by disturbed nervous function. Pulmonary and cardio-vascular disease often produce dramatic cerebral dysfunction.

Dietary deficiency such as those in thiamine or nicotinic acid deficiency states are common examples of metabolic disturbances which produce psychic manifestations.

Trace metal metabolism is an area in which expanding knowledge indicates the importance of minute quantities of certain of the metallic irons for the integrity of enzymatic functions intimately related to cerebral metabolism. Of interest are recent studies which indicate that repeated exposure to high concentrations of alcohol may result in depletion of zinc with impairment of dehydrogenase activity in the liver and hippocampal area of the brain.

Disorders of transmission of neural impulses such as were first recognized in relationship to acetylcholine at the ganglionic sites in peripheral nerve function is now recognized as also active in central nervous system synaptic function and may be responsible for certain emotional alterations. The brain and nervous system, despite the placid and pallid appearance of these structures, participate in very delicately balanced thermo-dynamic processes which are continually active. Tonus is determined by active neuronal participation for contracture and relaxation of muscular structures.

The frontal cortex, is now thought to exert more a modifying influence of an anticipatory or planning type rather than being the site for actual elaboration of those impulses and responses which are recognized as being emotional. Human observations and animal experiments in recent years indicate that the frontotemporal cortex area of the brain in association with various specific sites of the limbic system are responsible for emotional reactions and concomitant autonomic responses.

Although specific emotions may be enumerated in a rather lengthy list with some overlapping, it appears that all may be placed in two actually well defined categories, namely those which relate to self-preservation and those which relate to preservation of the species. Changes in emotion are accompanied by a variety of physiological alterations such as those related to temperature regulations, cardiac rate and rhythm, vasomotor responses, and changes in tonus of muscle in various structures of the body. It may be considered that the changes whioh are going on are representative of or a symbolic representation of information which the individual, in terms of human biology may have utilized in a more overtly expressive manner in an earlier evolutionary stage as indicators or signals of his response to an emotional stimulus. The vegetative nervous system is intimately associated with the transmission of impulses both for the initiation and regression of such activity, and should not be thought of in terms of autonomic response but reacts to higher brain centers of stimulation.

A better understanding of the internal environment or homeostasis and the effects of distant structures and their inter-relationships on cellular metabolism combined with the newer knowledge of neuro-physiology and neuralpharmacology are fields which are rapidly rendering obsolete the division of disease concepts into the organic and functional, and provide the framework of area for all aspects of human behavior to be related to a unitary concept; the end result of all disease in some degree relates to derangement in function.

PLASMA SUBSTITUTES

A REVIEW

W. L. THOMPSON, M. S.
Department of Pharmacology and Therapeutics
Medical College of South Carolina

Introduction

Transfusion of whole blood or pooled plasma represents the theoretically ideal replacement therapy in most hemorrhagic or shock states. Adverse features, however, such as limited availability, brief storage periods, typing reactions, virus transmission, etc. continue to direct interest toward substitute products. The inadequacies of low molecular weight crystalloids such as saline and glucose have been well recognized. High polymer colloids have been used for 60 years in conditions which do not require immediate infusion of blood cells. Plant and animal colloids are cheap, stable and can be sterilized but they frequently produce histamine-release reactions, hemostatic defects, clumping of blood elements, tissue storage with associated pathology, etc. When such reactions are reduced to an acceptable minimum, as might be the case with dextran at the present time, consideration can be given to the development of variations with different half-lives in the circulation. For example, a relatively short half-life is most suitable when a plasma substitute is used as interim therapy until whole blood can be obtained. A long half-life under these circumstances can lead to hypervolemia following the blood transfusion and this in turn can cause congestive heart failure if the myocardium has been significantly weakened. The following review is intended to present experimental and clinical experience with the more important colloids which have been used in the past, are being used at present or give prospect of future use.

ACACIA

Acacia or gum arabic is obtained from the sap of the African acacia tree and consists of arabinose, galactose, galactosoglucuronic acid and rhamnose in the form of calcium, magnesium and potassium salts. Its molecular weight is about 1500 but it is highly aggregated in concentrated solutions with a number average particle weight of 17,000 to 120,000 as determined by osmotic pressure.[1] Solutions of acacia in saline were used experimentally before 1900 and extensively during World War I. Amberson[1] has reviewed the reports of its use in more than 1800 patients with favorable results. Bayliss[2] claimed the injection of acacia is not associated with any serious toxic effect, noting only an in vitro agglutination of erythrocytes. Even a recent report[3] has suggested that it is superior to polyvinylpyrrolidone in the expansion of blood volume following hemorrhage in rabbits. However, the administration of acacia to bled dogs results in a mortality rate as great as in untreated animals.[4] Studdiford[5] noted tachycardia, cyanosis, dyspnea, pulmonary edema and 2 deaths in the administration of acacia to 3 patients. He observed similar reactions in dogs accompanied by aggregation of erythrocytes and increased erythrocyte sedimentation rate (ESR). The intravenous administration of acacia results in transient but profound hypotension in dogs[6, 7] and respiratory distress in guinea pigs.[8] Although Amberson[1] suggested that these reactions were caused by the use of impure samples, a recent report[9] has demonstrated that the hypotension which follows the injection of acacia in dogs is at least partially mediated by a massive release of histamine. In this report[9] it was observed that hypotensive reactions to initial injections of acacia conferred immunity to subsequent injections for several days but that clumping of erythrocytes was not prevented during this tachyphylactic period. Accompanying the hypotension and clumping there is a fall in the oxygen content of blood which has been ascribed to a coating of the erythrocyte interfering with its oxygenation.[10] A defect in the hemostatic mechanisms also occurs as evi-

denced by an increase in bleeding time.[11-13] Furthermore, acacia although it contains calcium has the capacity of adsorbing more calcium from blood and additionally altering its potassium and magnesium concentrations.[14] When injected, acacia is not metabolized but is stored in the liver, spleen, lymph nodes, kidney and bone marrow.[11, 15-18] This storage phenomenon is associated with liver damage greatly reducing the formation of plasma proteins and retarding their regeneration following hemorrhage.[12, 13, 16-19] Furthermore the formation of foam cells and atheromatous lesions with large doses has been described.[11] The clinical and experimental experience with acacia has been well reviewed by Gropper et al.[20] The discovery of more efficient and less toxic colloidal solutions has resulted in the clinical abandonment of acacia although it is occasionally used experimentally as a suspending agent for intravenous administration of insoluble substances.

METHYLCELLULOSE

The parenteral administration of methylcellulose has not been strongly advocated although at least one group[21, 22] has suggested its use as a plasma substitute. They noticed however that repeated administration of small doses produced anemia, increased plasma viscosity, increased ESR, persistent myeloid leukocytosis and prolongation of coagulation time. Furthermore, it is subject to tissue storage and produces a thesaurosis characterized by foam-cellular atheromatous changes in the arteries of rabbits and dogs similar to that caused by acacia. The storage phenomenon is also evidenced by prolonged anemia, leukopenia or leukocytosis, impaired coagulation and hemorrhagic diathesis, thrombopenia and a marked decrease in serum albumin and globulin.[11, 22, 23] Heuper[11, 23] has suggested that the mechanism involved in the production of the atheromatous lesions is the formation of films which interfere with the oxygenation of vessel walls. Similar reactions and thesauroses have been described following injections of hydroxyethylcellulose.[24] In a recent investigation[9] small injections of methylcellulose produced rapid fatalities in dogs by what appeared to be an obstructive phenomenon related perhaps to the extremely high viscosity of methylcellulose solutions.

PECTIN

Pectin is a mixed polysaccharide composed of acetic acid, arabinose, galactose, galacturonic acid, methanol and xylose.[25] It has a molecular weight of 100,000 to 250,000 but can be fractionated by autoclaving to more suitable molecular weights.[26] Its use as a plasma substitute was suggested during World War II[25] and in a report of its use in 155 patients[27] storage in spleen, kidneys, liver and lungs was noted. The review by Gropper *et al*[20] suggests that pectin is retained in the circulation at least 4 hours after injection but is cleared within 7 days. However, others have reported prolonged storage[28, 29] producing foam-cellular atheromatosis.[28, 30] The administration of pectin solutions to bled dogs results in 100% mortality.[4] Its administration increases capillary permeability and produces hypoprothrombinemia, hypofibrinogenemia and thrombocytopenia.[31] Extreme reactivity, storage and low efficiency have prevented clinical acceptance of pectin solutions.

HEMOGLOBIN

The use of solutions of hemoglobin in saline has been reviewed by Amberson.[1] Human hemoglobin in saline has been shown to be superior to dog plasma in supporting the circulation following moderate hemorrhage in dogs.[32] However, its rapid conversion to methemoglobin and disappearance from the circulation, interference with renal function, storage in liver and spleen, production of increased ESR and other toxic effects have prevented extensive clinical use.[1, 20, 26]

MODIFIED HUMAN GLOBIN

The use of human globin extracted from erythrocytes as a plasma substitute has been suggested by Strumia.[33] The derived protein has a molecular weight of 34,000 and 30 Gm of globin can be obtained from one pint of blood as compared with 15 Gm of plasma protein.[26] From the red cells now discarded it has been estimated that 6,000,000 16 Gm units of globin could be obtained.[26] Gropper *et al*[20] have reviewed its use in 108 patients without reactions. In the dog, however, globin pre-

pared from dog blood has been found to produce respiratory distress and symptoms of histamine release.[32] It is much less effective than saline in supporting the circulation of dogs following hemorrhage.[33, 34] Globin has been discarded as a plasma substitute and finds no clinical use today.

GELATIN

Hogan[35] in 1915 reported on the administration of gelatin to 7 patients in shock. The solution seemed to be of benefit and no deleterious effects were noted. The interest in gelatin during World War I was not great however due to the antigenicity and the possible transmission of tetanus and anthrax.[28] There are several commercial brands of gelatin for parenteral use currently available, most of which are derived from the collagen of the hard bones of cattle and fractionated by autoclaving to average molecular weights below 40,000.[36] It would seem that a protein would be an ideal colloid for use as a plasma substitute as it would be similar to plasma proteins.

It has been reported that gelatin does not maintain blood volume as adequately as dextran in bled rabbits and in normovolemic patients[3, 36] but the efficiency of gelatin as a plasma substitute seems to vary greatly with the method of assay. An excellent measure of the usefulness of volume expanders is the bleeding volume index (BVI). To determine the BVI an animal is bled to a specific end point and then the colloid is infused either immediately or after a period of hypotension. After a specific time interval the animal is bled to the same end point again and the ratio of the volume of blood obtained at the second bleeding to that obtained initially is the BVI. In a study of the efficiency of plasma substitutes in dogs utilizing BVI,[24] gelatin was found to be superior to plasma and polyvinylpyrrolidone (PVP) but inferior to dextran and albumin. In a study of survival following hemorrhage and replacement in dogs,[37] gelatin appeared superior to dextran and PVP. In this study it was found that if gelatin were used as the replacement fluid, the hemoglobin concentration could be reduced to 20% of control with a survival of greater than 50%. In another survival study[4] gelatin had a survival rate of 60% as compared with 94% with heparinized plasma, 74% with serum, 50% with citrated blood, 42% with saline, 30% with citrated plasma and 12% untreated. Using serial hemorrhages and replacement, Levinson *et al*[38] noted excellent results, with hemodilution the only deleterious effect. One defect of gelatin seems to be that it is rapidly eliminated from the circulation. When one liter of 5% osseous gelatin is infused into patients at a rate of 300 ml/hour, only 55% of the injected gelatin is present at the end of the infusion and the plasma levels decline from 780 mg/100 ml at the end of the infusion to 300 mg/100 ml at 24 hours.[39] This might suggest the use of gelatin infusions for parenteral alimentation but the same article indicates that 80% of the infused gelatin is excreted within 72 hours, the excretion continuing for several days thereafter. Thus there is little or no catabolism of this colloid. Normal renal function is not necessary for the elimination of gelatin from plasma as the rate of decay of plasma gelatin concentrations is the same in normal and oliguric patients.[40] Gropper *et al*[20] in an extensive review of clinical reports conclude that gelatin is equivalent to plasma in the expansion of blood volume and survival following hemorrhage but note that there is some controversy as to its superiority to normal saline in burn shock.

There has been some discussion of the possibility of antibody formation to gelatin. Maurer[41] has shown that there are normally occuring antibodies to gelatin in human serum and in the serum of the dog and other animals.[42] The content of gelatin in the diet does not influence the antibody content of dog and rabbit serum.[43] These antibodies do not appear to have great clinical significance as there have been no reports of serious anaphylactic reactions to infusion of commercial gelatin. A recent investigation[8] has shown that injections of 100 to 200 mg/kg of Plazmoid gelatin in normotensive dogs produce occasional brief moderate hypotensive reactions. The possibility of serum sickness following gelatin infusions remains an important consideration in the administration of these solutions.

Gelatin seems to be relatively non-toxic in comparison to some of the other colloids. Behrmann[31] noted that gelatin infusions are not followed by increases in capillary permeability as observed following infusions of pectin, methylcellulose, dextran and PVP in dogs. Gelatin produces only slight pathological changes in patients[27] and Hueper[11] has reported that it does not produce the foam-cellular atheromatous thesaurosis typical of acacia, pectin and methylcellulose. Another group[45] has reported some atherosclerotic changes and interstitial nephritis upon repeated administration of gelatin to dogs. Hartman[28] has reported a gelatin nephrosis of short duration in mice and Skinsnes[46] noted frequent appearance of swollen kidneys with histological changes in the tubules of 32 patients who died after receiving 100 to 17,600 ml of gelatin. This appears to occur within one-half hour of the infusion and the kidney is restored to normal within 5 days. There is a close resemblance between this gelatin nephrosis and that produced by sucrose[47, 48] and may be caused by absorption of gelatin into the tubule cells where it is then followed by water.[46] The degree of renal impairment associated with this nephrosis is not clear however as Ravdin[49] reported no change in glomerular or tubular function following administration of gelatin to dogs for 112 days and 1 to 2 liters of gelatin each day for one week to volunteers. Another study of normovolemic or bled volunteers[50] showed that hemodilution was the only ill effect of gelatin infusion.

Following gelatin infusions, aggregation of erythrocytes is greatly increased. Miller and Little[51] have demonstrated the formation of flexible clumps of erythrocytes which break up readily. Another group[52] observed increased ESR in dogs infused with gelatin. Perhaps the most extensive study of erythrocyte aggregation by gelatin has been made by Thorsén and Hint[53] who showed that 18,000 was the minimum molecular weight producing increased ESR and that the ESR is proportional to the molecular weight and concentration of gelatin. They also demonstrated the formation of a surface film on the blood cells following infusion.

Although there is some clinical use of gelatin solutions today, there seems to be a declining interest in unmodified gelatin.

MODIFIED FLUID GELATIN

A major inconvenience in the use of gelatin is that it is solid at room temperature and must be warmed before and during infusion. An attempt to eliminate this feature has been the development of a chemically modified heat-degraded gelatin—modified fluid gelatin (MFG) which is fluid at room temperature. In terms of the BVI, MFG appears to be slightly inferior to dextran when infused immediately following hemorrhage but superior to it when administered after a 60 minute period of hypotension at a mean blood pressure of 30 mm Hg.[54] A clinical study[55] of MFG has shown that the plasma concentration has decreased to one-third of control 4 hours following infusion but that the volume expansion has only been reduced to two-thirds of control. Another group[56] has found that 91% of infused MFG is retained after 4 hours and 88% after 24 hours. They also found that following hemorrhage and a period of hypotension MFG is about equal to autogenous blood as determined by BVI. Ravdin[57] has demonstrated a retention of 90% of the infused volume of MFG at 12 hours in oligemic volunteers. The retention was only 10% if they were normovolemic before infusion, indicating the importance of pre-infusion volemia in determining the persistence of plasma substitutes. Increases in capillary permeability following hemorrhage and replacement with MFG have been reported[58] to be associated with reduction in prothrombin, platelets and fibrinogen and prolongation of bleeding times. Modified fluid gelatin is not in widespread use today.

OXYPOLYGELATIN

Another attempt to modify gelatin has been to utilize condensation with glyoxal followed by oxidation with hydrogen peroxide producing oxypolygelatin (OPG) which is fluid at 10 to 13° C. When this product is administered to bled rabbits, 25 to 50% is retained for 6 hours.[59] In normal subjects given OPG the plasma concentrations decreased from 500 mg/100 ml at the end of infusion to

200 mg/100 ml within 4 hours.[60] Although this study showed good results using OPG in patients in shock, 5 of the 42 normal subjects experienced allergic reactions. In a review of several articles, Gropper *et al*[20] conclude that OPG is retained about 37% at 5 hours and 14% at 24 hours accompanied by a volume retention of 59% at 5 hours and 32% at 24 hours. Studies of survival in bled rabbits and dogs treated with OPG indicate that OPG is superior to plasma and dextran in rabbits[61] and superior to dextran and PVP in dogs but inferior to Plazmoid gelatin and plasma in dogs.[37] Studies of BVI have shown that OPG is superior to plasma but inferior to blood in dogs[62] and that it is inferior to dextran and MFG when replaced immediately following hemorrhage or after a period of hypotension.[54] Increased ESR[52, 60] and agglutination of erythrocytes[61] have been observed following OPG infusions. A careful study of the aggregation of erythrocytes by OPG has been carried out by Feigen and Campbell[62] who concluded that OPG is attached to cells by proton bonds and that the increased ESR is caused by interaction of long protein chains with reactive sites on the cells. They showed that sodium salicylate prevents this aggregation and suggest that this protection is mediated by a reaction of the salicylate with both the protein and the cell sites.

ISINGLASS

Isinglass, a gelatin derived from fish swim bladders, has been used without serious deleterious effects in patients.[63] The supposed advantage is avoidance of contamination by tetanus and anthrax. Gropper *et al*[20] in reviewing its use noted a 14% reaction rate in man.

BOVINE SERUM ALBUMIN

Bovine serum albumin has been given to 410 patients with 12 immediate anaphylactoid reactions consisting of hypotension and dyspnea or pyrogenic reactions and 38 delayed reactions with urticaria, erythema· arthralgia, fever, myalgia, etc.[64] Gropper *et al*[20] in reviewing the reports of infusions of bovine plasma noted a 15% reaction rate. Their review of extensive studies of deantigenation is not encouraging and this problem may well be the one factor preventing widespread use of the many animal proteins which are readily available.

POLYVINYLPYRROLIDONE

Early in World War II, Hecht of the Bayer Company in Germany began research which led to the development of a new synthetic plasma substitute — polyvinylpyrrolidone (PVP).[65] PVP is synthesized from acetylene, ammonia and formaldehyde under pressure. The original product had a weight average molecular weight of 25,000 but the current American products have molecular weights between 33,000 and 56,000.[20] Renal excretion of PVP with a molecular weight of 15,000 or less is very rapid, but there is a sharp cutoff at 35,000 to 40,000.[20] Urinary excretion in patients has been estimated to be about 40% in 24 hours with a total excretion of not more than 60%.[66] The efficiency of PVP as determined by BVI seems to be very low in dogs—ranking less than plasma and OPG and being superior only to saline.[54] PVP has been found to be inferior to gelatin and dextran in volume maintenance in bled rabbits.[5] In terms of survival it is inferior to gelatin and OPG and superior to dextran.[37]

Reactions to PVP manifested by increased ESR[67, 68] and hypotension and death in dogs[69] are frequent. Pretreatment with 35 ml/kg does not prevent dogs from reacting to to 350 ml/kg. Graded doses of 8 to 210 ml/kg administered in 2 to 14 injections does decrease the response to larger doses. Pretreatment with massive doses gives almost complete protection against later injections. When the blue dye T1824 is injected before PVP, the intense erythema is accompanied by intense bluing.[70] Dialyzed PVP does not cause hypotension in tolerant dogs but the gross external signs appear. The response is characterized by vasodilation and hemoconcentration by increased permeability.[70] These effects have also been noted by Halpern *et al*[71] who reported that promethazine inhibits to some extent the increased rates of water and protein filtration through capillary walls. PVP administered intraperitoneally is 100% absorbed in the rabbit within 8 hours and 90% absorbed in the dog within 9 hours. Although the ESR increased 11 fold in rabbits and 5 fold in dogs,

there were no other manifestations of an anaphylactoid reaction and this method of administration has been proposed for patients in cases where intravenous infusion would be impossible or impractical.[73] Loubatières[78] reported shock and loss of consciousness following injections of 175 mg/kg in dogs and hypotension to 40% of control blood pressure with 750 mg/kg. He also noted an increase in coagulation time to 25 minutes. Halpern and Briot[74] have demonstrated an increase in plasma histamine from less than 20 microgm/l to above 350 microgm/l following administration of PVP to dogs. The increase in plasma histamine persisted for greater than 30 minutes and was accompanied by a decrease in blood pressure to 20 to 60 mm Hg. They also noted a large increase in the volume of gastric secretion and the concentration of free acid. Itching, edema, shock, hemoconcentration and refractoriness for 2 to 3 days followed the reaction. Administration of 1 to 18 mg/kg of PVP to dogs results in variable responses, but severe hypotension, hemoconcentration and skin flushing invariably follow the intravenous administration of 105 mg/kg.[75] The small molecular weight fraction (20,500) is active but the very large molecular weight fraction (560,000) is inactive in producing these responses.[75] A recent report from this laboratory[9] has demonstrated that doses of 1 to 350 mg/kg in dogs cause severe shock and that the response increases with increasing dosage. This response frequently persists for longer than one hour and is accompanied by increases in plasma histamine from control values of less than 63 microgm/l to levels of 2100 microgm/l. This response has been termed a "canine" reaction and thought by some to be species specific. However it is highly probable that the dog is not unique but only more sensitive. High molecular weight (1,000,000) PVP is antigenic in man causing specific antibody formation.[76, 77] This does not necessarily indicate that clinical PVP is antigenic and anaphylaxis probably plays no part in the reactions to PVP seen in the dog.

In the mouse 15 to 16% of injected PVP can be found in the carcass after 58 days. Most of this is in the pelt but some is in the liver, muscles and bones.[78] Fractions of molecular weight 110,000 to 120,000 are stored for years although fractions of molecular weight 40,000 or below are excreted within a few days.[79] The severity of this prolonged storage has been demonstrated by studies of radiochromic phosphate capture by the reticuloendothelial system in rabbits given 350 mg/kg of PVP weekly for 12 weeks. Six weeks after the end of this procedure the rate of uptake of the chromic phosphate is 59% of control.[80] Rabbits given 16 injections of 350 mg/kg of PVP show splenomegaly with foam cells constituting one-third to one-half of the spleen and other storage phenomena in lymph nodes, bone marrow, adrenal medulla, lungs and blood vessels persisting in the reticuloendothelial system and endothelium for more than 4 weeks. This causes thrombosis and penetration of capillary walls with formation of granulomatous consolidation of the lung parenchyma.[29] Hartman[28] indicated that German army pathologists found damage to liver and kidneys in soldiers to whom PVP had been administered and advised against further use. Gropper *et al*[20] note that PVP has the capacity to bind certain molecules and reduce their absorption or excretion. They reviewed the use of PVP to retard the absorption of penicillin, insulin and other drugs and noted that it may be capable of binding toxins from diphtheria and clostridia and even viruses. In reviewing the literature they concluded that no reactions upon administration of PVP to man occur except in infants under 2 years of age. Drill[24] noted that one study has indicated no effect of PVP on renal or hepatic function in man even when administered in volumes up to 3,000 ml. Drill also noted that PVP may give false positive tests for albuminuria and contribute to the blood "sugar" as determined by reducing tests.

PVP was an innovation in the field of plasma substitutes by virtue of its synthetic source. The tissue storage reactions have prevented more widespread use of this substitute and it is rarely used in this country at this time.

POLYVINYLALCOHOL

Gropper *et al*[20] reviewed several reports of the use of polyvinylalcohol (PVA) which ap-

pears to be inferior to PVP in the maintenance of blood volume following hemorrhage. Following the intraperitoneal or intravenous administration of PVA to dogs, atheromatous lesions of the aorta and carotid and femoral arteries develop which resemble cholesterol atheromatosis.[82] Hueper suggested that PVA disturbs the oxidative metabolism and nutrition of vascular walls producing the lesion.[82] In rats and rabbits PVA produces foamy cytoplasm histiocytes in skin, lungs, lymph nodes, Kupffer's cells and is even stored in neuroglia and ganglion cells of the brain.[83] This storage in the central nervous system is not seen with PVP which is excluded from the brain.[79] The endothelium of many vessels is covered by a layer of PVA which is accompanied by the development of proliferative and obliterative arteriolar lesions. The capillary endothelium in renal glomeruli are filled with swollen cells obliterating the lumen. This reaction also follows administration of acacia, methylcellulose and pectin.[23] Administration of PVA causes increased ESR, aggregation of erythrocytes and increased coagulation time.[84] There has been no serious consideration of clinical use of PVA because it appears to be much less effective and more toxic than PVP.

DEXTRAN

Dextran was first recognized as a contaminant formed in the juices of sugar beets and other food products. In the nineteenth century it attracted attention by obstructing pipes through which sucrose juices were transported. Scheibler in the 1870's determined that is was a polymer of anhydroglucose units.[85] Dextran is formed from sucrose by the action of *Leuconostoc mesenteriodes* and similar microorganisms. During the reaction fructose is split off from the sucrose leaving glucosyl radicals which react with the non-reducing end of growing chains. Free fructose is liberated in the reaction but very little free glucose is formed.[86] The synthesis does not require the mediation of any phosphorylated sugar[87] and can be carried out in the presence of a cell-free suspension of dextransucrase.[88] The basic structure of dextran is a branched polymer of alpha 1, 6 linked D-glucopyranose units. At points of branching there may be 1, 3 or 1, 4 bonds. The degree of branching is dependent on the strain of the organism as well as the culture characteristics. Dextrans are characterized by a high degree of polydispersity. Native dextran produced by strain NRRL B-512 of *L. mesenteroides* has a molecular weight greater than 10,000,000. The molecules vary greatly in size and are branched flexible coils. Native dextrans produce very viscous solutions which mix poorly with water and are unsuitable for parenteral use. When injected as 1 to 3% solutions they cause death of experimental animals by diffuse thrombosis of small vessels.[85] The native dextrans are degraded by heat as the molecular size is monitored by viscosity or alcohol precipitation. Other methods of depolymerization include ultrasonic vibration, alternating electrical fields, gamma irradiation and the enzyme dextranase found in several microorganisms. After the dextran is degraded it is fractionated by alcohol precipitation which is not sharp and the resulting fractions are relatively inhomogenous. If the number of individual molecules is determined by osmotic pressure or the number of reducing end groups the number average molecular weight can be derived. If physical constants of the colloid are determined such as intrinsic viscosity, sedimentation rate, light scattering, etc. the resulting information can be compared with other constants for similar solutions to obtain the weight average molecular weight. Low molecular weight particles have more influence on the number average and high molecular weight particles have more influence on the weight average molecular weight. Thus the weight average is always greater than the number average and the ratio of weight average to number average is a measure of polydispersity. Intrinsic viscosity is a measurement which is convenient and rapid but the regression of intrinsic viscosity on molecular weight varies greatly with the extent of branching and molecular dimensions. For dextran of a particular strain which is degraded and fractionated by carefully controlled procedures, intrinsic viscosity can be used to indicate molecular weight after more careful sedimentation equilibrium studies have been used to obtain the viscosity-molecu-

lar weight relationship. The American specifications now direct that the dextran must be fractionated by methanol precipitation so that the 10% containing the heaviest molecules and the 10% containing the lightest are separated. The weight average molecular weight of these two fractions must be determined by light scattering. The high 10% fraction must have a weight less than 200,000 and the low 10% fraction must have a weight greater than 25,000. The clinical preparation now manufactured at Pharmacia Ltd., Uppsala from a B-512 strain has a mean molecular weight of about 75,000 by light scattering. A fraction of this dextran with a molecular weight of 69,900 has been found to contain molecules which are roughly 3 times as long and one-half as broad as serum albumin. This dextran when purified is a faintly yellow powder which is soluble in water to 20%. Currently Sweden specifies that the weight average molecular weight by light scattering must be 80,000 ± 10,000, the intrinsic viscosity between 0.24 and 0.27, the nitrogen content less than 1 mg/100 ml, the pH between 4.0 and 7.0 and that it must be in a solution containing 0.9% sodium chloride or 5% glucose. (The above discussion has been largely derived from Grönwall[85] who has thoroughly reviewed the literature relating to the clinical use of dextran.) A 6% solution of clinical dextran manufactured by the Commercial Solvents Corporation has a viscosity of 2.5 to 3.5 centipoise at 25° C. In this country number average molecular weight is determined from the number of terminal anhydroglucose units, which contain a carbonyl group. The use of intrinsic viscosity is discouraged because of its dependence on polydispersity which varies with each sample.[89]

Grönwall and Ingelman investigated the possible parenteral applications of degraded dextran during World War II.[90] They discovered that dextran solutions were the best plasma substitutes known at that time and initiated clinical usage which has grown steadily since their early work. The clinical result obtained with dextran is dependent upon the rate of its elimination from the blood and therefore upon the rate of its excretion into urine and its passage into lymph. This in turn is almost solely determined by molecular weight as dextran is excreted solely by glomerular filtration without substantial tubular reabsorption.[91] Two hours after administration of dextran to nephrectomized animals the plasma levels are 30% of control with fractions of molecular weight 10,600; 70% with 35,000; 85% with 91,700; and 90% with 135,000 to 412,000.[94] The plasma/lymph gradient is inversely proportional to molecular weight but even the 412,000 fraction penetrates the capillaries. The plasma/lymph gradient decreases as the amount infused increases[94] and 4 hours after infusion 80% of the initial volume expansion is maintained in bled dogs but only 25% in unbled animals.[95] This clearly demonstrates the great difficulty in evaluating reports of the efficiency of plasma substitutes as the procedure used is very important in determining the result. A careful study in patients receiving 500 ml of clinical dextran has shown that the blood concentration of dextran declines from 700 mg/100 ml at the end of the infusion to 300 mg/100 ml after 24 hours and to 175 mg/100 ml after 48 hours.[96] Thus it seems that dextran fulfills the requirements of the U: S. National Research Council that 50% of the infused plasma substitute must be present in the blood at the end of 12 hours.

Wilson *et al* [97] reported excellent results with dextran in the therapy of oligemic and traumatic shock. Dextran is superior to OPG but inferior to plasma in the bled rabbit as determined by BVI and survival.[91] Another report has shown it to be superior to acacia, gelatin and PVP in the maintenance of blood volume in bled rabbits.[3] In bled dogs it is superior to gelatin, OPG, PVP and plasma and only slightly inferior to albumin and whole blood as determined by the BVI.[94] Following replacement of extensive hemorrhage by dextran in the dog, 50% of the protein loss is replaced within 4 days.[98] The administration of dextran to volunteers is associated with increased cardiac output and prolonged elevations in right atrial and pulmonary arterial pressures[99] along with hemodilution which is gradually corrected.[100] In normovolemic dogs infused with 10 ml/kg of dextran there is a decrease in total circulating serum albumin to

60 to 70% of control within 30 minutes. This effect does not occur with infusions of dextran in bled animals.[101] In bled dogs maintained at mean blood pressures of 40 mm Hg for 60 minutes, dextran is comparable to pooled dog plasma in maintenance of blood pressure.[102] The restoration of lost hemoglobin is as rapid with dextran as with plasma and in 12 days amounts to an increase of 40% of the erythrocyte mass at the end of hemorrhage. Plasma protein regeneration is not retarded and amounts to a 100% increase in plasma protein mass in 12 to 14 days.[102] The hemodilution and increased blood pressure seen upon infusion of dextran in normovolemic dogs is greater than that produced by saline or dextrose.[103] Thorsén however has shown that when dextran is administered the plasma volume may be increased, decreased or unchanged depending upon the preinfusion volume (greater expansion if hypovolemic), the colloidal osmotic pressure of the plasma (greater expansion if low colloidal osmotic pressure before infusion), and the amount of fluid outside the circulatory system (greater expansion if much available fluid.[104]) Meyer *et al*[105] infused 500 ml of 6% dextran into normal volunteers and measured an increase in blood volume of 960 to 2850 ml with a mean of 1880 ml occurring in 1/4 to 6-1/4 hours of the infusion. This unusual degree of expansion is partially explained by the observation of Pirani *et al*[102] that the colloidal osmotic pressure of 6% dextran is 50 to 100% greater than that of plasma.[102] Also, Thorsén has demonstrated that the colloidal osmotic pressure of a mixture of plasma and dextran is greater than that expected from their individual osmolarities.[104] Using serial hemorrhages in dogs and replacement with plasma or dextran, Wise *et al*[106] found that there is a compensatory increase in cardiac output and arteriovenous oxygen difference although oxygen consumption decreases. The mechanisms compensating for hemodilution are rapidly exhausted when the hemoglobin falls to 50% of control and at this level there is evidence of tissue hypoxia. This is probably related to the empirical standards established during the Korean conflict for the mixing of infusions of dextran and blood when treating casualties. Dextran alone was administered to a total volume of 1500 ml. If the infusion volume was 1500 to 4000 ml, dextran was administered equally with blood. If the volume was 4000 to 7000 ml, 2 units of blood were administered with each unit of dextran and the maximum dextran infusion was limited to 2½ liters.[107] In addition to its use in oligemic shock, dextran has been used in the hemoconcentration hypovolemia of burn shock.[108, 109] Dextran seems to be an entirely acceptable therapeutic agent in these cases although the concomitant use of plasma prevents the decrease in plasma proteins associated with the use of dextran alone. Clinical reports have repeatedly claimed satisfactory response to the use of dextran in many types of shock.[110] Acidosis however, is one factor in shock that is not as well treated with dextran as with plasma but this probably could be corrected by the addition of buffers to the dextran solutions.[111] Dextran is probably the most efficient artificial plasma substitute in use today and it is as acceptable as plasma in most cases.

In addition to urinary excretion, dextran is eliminated by catabolism. It has a metabolic half-life of about 6 days in mice. The carbon which is liberated is incorporated into the carbon pool, primarily in the lipids. Some of this carbon is excreted as carbon dioxide.[112] However, dextran does not appear to be converted into appreciable glucose in pancreatectomized dogs.[113]

An early report[109] noted a very low incidence of reactions (0.2%) in 25,000 infusions of dextran in Sweden. This has not been substantiated by more recent experience in which anaphylactoid reactions are common. Before changing to the use of the B-512 strain, there were 8% reactions to American dextran, 34% to Swedish dextran and 44% to British dextran.[114, 115] There have been numerous clinical reports of reactions to dextran.[116-122] This high incidence of reactions contrasts sharply with the statement of Thorsén in 1949 that he had observed a reaction rate of 0.4% with dextran as opposed to 8.2% with whole blood.[123] One possible explanation for this discrepancy is that the Swedish investigators did not report many of the minor types of reactions such as headache, chills, flushing, urticaria, wheezing,

angioneurotic edema, nausea, vomiting, cramps, chest pain, rhinitis, facial edema, joint pain, etc.,[116] which are the major symptoms seen by more observant investigators. Actually the B-512 strain was adopted in an effort to reduce the frequency of reactions. The original dextran had 88% 1, 6 linkages, 5% 1, 4 and 7% 1, 3 while the B-512 dextran has 96% 1, 6 and 4% 1, 3. The lower degree of branching with B-512 is thought to have contributed to the reduction in the frequency of reactions.[122] Similar reactions can be seen in animals. When rats are infused with dextran, swelling of the paws and generalized edema are observed. This is primarily mediated by 5HT although histamine is involved.[124] There is some cross protection between dextran and 48/80, an agent producing severe anaphylactoid reactions.[125] When rabbit blood cells are mixed in vitro with dextran, histamine is released and this release is proportional to the molecular weight and concentration of the dextran.[126] A recent investigation[9] has demonstrated that dextran provokes a histamine release in the dog which is not accompanied by hypotension. This histamine release is quite small in magnitude when compared to that produced by acacia and PVP.

There has been some interest in the antigenicity of dextran. There is a reaction between dextran and leuconostoc antisera. Dextran also crossreacts with types 2, 12 and 20 antipneumococcal sera[127] and that from some salmonella and streptococci[128, 129] Dextran is a haptene in rabbits even when it is purified to a nitrogen content of less than 0.08%.[130] In man precipitins are formed and cutaneous sensitivity develops after the injection of 1 mg of a high molecular weight dextran.[131] There are skin reactions to dextran in many persons who have not received dextran injections.[132] Human sera from persons who have not received dextran frequently contains specific precipitins to dextran. The reaction rate to dextran is higher in those persons who have more than 2 microgm/ml of dextran-precipitable antibody nitrogen.[122] Reactions are also more frequent among those who have the greatest increase in antibody nitrogen following inoculation.[133] The greater the proportion of non-1, 6 linkages to 1, 6 linkages the greater is the formation of antibodies following injection. Thus the use of B-512 dextran is associated with lessened antigenicity.[122] The molecular weight of dextran also contributes to the antigenicity and antibody formation which is greater with a fraction of 150,000 molecular weight as compared with a fraction of 30,000.[134] The significance of this antigenicity is difficult to determine. Dextran can precipitate plasma proteins and this observation tends to discredit results of antigenicity studies in which the quantity of nitrogen precipitable by dextran is measured. Undoubtedly high titers of antibodies may contribute significantly to a reaction to dextran. However, it is probable that there are few reactions to dextran caused entirely by antibodies. The reactions which are seen following dextran are probably the same type of anaphylactoid reactions seen with other colloids in which antibodies play little or no role.

Infusions of dextran do not decrease the concentrations of plasma constituents equally. Serum globulin and cholesterol are reduced more than albumin and this persists after the dilution is no longer apparent.[135, 136] Dextran decreases fibrinogen concentration in excess of that expected by dilution. In dogs infused with dextran, fibrinogen decreases from 207 to 79 mg/100 ml in 15 minutes while albumin decreases from 2.81 to 1.33 Gm/100 ml.[137] Dextran also precipitates fibrinogen in vitro.[138] Dextran, acacia and PVP form insoluble complexes with fibrinogen at 4° C but not at 37° C[139] but the significance of this complex is not clear.

The effects of dextran on plasma proteins are important from another viewpoint. Dextran increases the ESR both in vitro and in vivo[67, 72, 100] Accompanying this increase in ESR there are minor difficulties encountered in blood typing.[140-142] The increased ESR is also associated with increased intravascular aggregation of blood elements.[9, 61, 143] Swank[144] has shown that the injection of dextran in dogs causes aggregation of erythrocytes and slowing of blood flow by formation of amorphous films enveloping the cells. He relates the decrease in fibrinogen seen following dextran with the decrease in platelets and increased clumping of cells by suggesting that

a fibrinogen-dextran complex is formed which constitutes the film covering the cells and that this increases their adhesiveness.[144] He noted manifestations of neurological impairment in conscious dogs and suggests that this may also be due to a coating of the cells and endothelium with a fibrinogen-dextran complex decreasing the effective oxygenation.[144] The effects of dextran on the viscosity of the blood have also been related to this neurological deficit. Dextran increases the viscosity of blood in relation to its molecular weight. If the molecular weight is greater than 81,400, paralysis is noted. This is more closely related to increases in blood viscosity. The normal viscosity of blood is 4.5 centipoise. If this increases by 2.0 centipoise following dextran the dogs become paralyzed. If the increase is less than 1.4 centipoise there is no paralysis. Electrocardiographic indications of myocardial hypoxia occur with the paralysis and these revert to normal within one week. Swank suggests that this increase in blood viscosity may be extremely serious in certain patients, especially those with arteriosclerosis.[145] Thorsén and Hint in their extensive study of ESR noted that dextrans of molecular weight 59,000 and above produced increases in ESR.[53] However, the presence of low molecular weight dextran prevents or decreases the effects of the high molecular weight dextrans.[53] Hardwicke[146] has suggested that ESR is dependent upon the fibrinogen concentration and upon a serum factor. He notes that increased fibrinogen concentration will increase ESR and that fibrinogen levels are elevated in most conditions associated with increased ESR. He also noted the relation of dextran molecular weight to its effect.[147] This is consistent with the belief of Swank that the fibrinogen concentration at the surface of the erythrocyte is elevated by the deposition of a fibrinogen-dextran film. This concept is further supported by the observation that platelets suspended in protein solutions are coated with the proteins and that their isoelectric point shifts toward that of the protein. When dextran is added to such a mixture, there is a significant alteration in the mobility of the platelets and a decrease in their isoelectric point.[148]

Weil and Webster[149] observed an increase in the coagulation time of blood accompanied by a decrease in fibrinogen and platelets following addition of dextran to human blood in vitro. With large doses of dextran other investigators have reported prolongation of bleeding times which closely paralleled dextran levels.[150] In some patients there is hematuria in the absence of albuminuria.[151] Adelson[152] observed an increase in bleeding time in 46% of patients infused with one liter of dextran. The hemostatic defect is proportional to the molecular weight of the dextran and reaches its peak at 3 to 9 hours following the infusion. Clotting time is also prolonged by dextran and this is proportional to the molecular weight and the concentration of the dextran both in vitro and in vivo.[153] Adelson *et al*[154] have postulated that the increased bleeding time is a platelet effect. They found that thrombocytopenic dogs and patients are more sensitive to dextran and that the increase in bleeding time closely corresponds to the decrease in platelets. Dextran has been shown to inhibit threone activity which would tend to inhibit prothrombin activation.[155] Since threone is a combination of platelet clotting factors this evidence may support Adelson's belief. The most extensive study of the effect of dextran on the clotting mechanisms has been made by Jacobaeus.[156] He demonstrated that infusion of dextran reduces the prothrombin consumption in normal volunteers and that in several it was totally inhibited. This decrease in prothrombin consumption is greatest with the high molecular weight fractions and fractions with molecular weights of 41,000 are inactive. Fractions with low molecular weights actually increase the prothrombin consumption. As the molecular weight of the dextran is increased there is a decrease in platelet activity. Jacobaeus postulated that a platelet factor leaks out of the platelets and the higher molecular weight fraction causes faster leakage. The hemostatic defect is not seen until the supply in the platelets is exhausted or the leakage becomes too slow to make up for the inactivation of the factor free in the plasma. To explain the delay in appearance of the bleeding defect he postulated that the smaller molecules which increase prothrombin consumption prevent the

appearance of the prothrombin consumption inhibition by the larger molecules. The effect then becomes apparent when the smaller molecules are filtered and lost from the circulation. No bleeding defects were noted in 200,000 infusions of dextran early in its use. The original dextran was shorter and more branched than the modern B-512 and Jacobaeus has suggested that this change may have had some influence on the effect of dextran on the hemostatic mechanisms.[156]

The major objections to the use of acacia and PVP are the storage phenomena and associated pathology occurring after their injection. It was believed that dextran would not exhibit these effects because its constituents were more closely related to the normal body components. Although the pathology associated with the injection of dextran is much less than that seen with the other colloids, tissue changes are not altogether absent. Following dextran administration in dogs and rabbits the epithelial cells of the tubules of the kidney are swollen, vacuolated and granular and the lumens of the tubules are filled with debris. This effect is transient, persisting less than 5 days.[157] In mice storage is marked in the liver, renal tubules and reticuloendothelial system.[158, 159] In Korean casualties given dextran, its presence was marked in the spleen, myocardium and liver and the renal tubular cells were swollen and vacuolated resembling sucrose nephrosis.[160] These pathological findings are not very significant as there is little or no decrease in renal function following administration of large amounts of dextran.[95, 97] Dextran is concentrated in the liver and lymph nodes but is converted fairly rapidly to glucose and utilized for energy with 6 to 25% excretion as carbon dioxide.[161-163] The more rapid metabolism of dextran may explain the transient changes associated with its storage in contrast to the permanent pathology which occurs with acacia and PVP.

The production of dextran in this country is rather limited considering its possible application. The total American civilian consumption in 1957 was 150,000 units. At that time the Federal Civil Defense Administration had 3,475,000 units stockpiled and the Department of Defense had about 1,400,000.[164] This stockpile would be entirely inadequate in a major disaster. The major limitation to more widespread use of dextran is its price. Dry bulk dextran costs $13.00 per pound, but when this material is degraded, fractionated, tested, bottled, sterilized, transported and stored the wholesale price becomes $6.50 to $6.80 per unit of 500 ml of the 6% solution.[164]

HYDRODEXTRAN

In an attempt to prevent reactions and hemostatic defects, Harrison *et al*[165] reduced the terminal aldehyde groups of dextran to primary alcohol groups. This product was called hydrodextran and was produced under the trade name of Hydrox by the J. T. Baker Company. It appears to be quite similar to unmodified dextran and 50% is excreted within 24 hours of administration to patients in shock. The plasma levels decline from 1860 mg/100 ml 30 minutes after the administration of one liter to 834 mg/100 ml at 24 hours.[166] There does not appear to be any benefit associated with this modification of dextran and as it involves the additional process of boron removal by ion exchange resins, it is probable that the increased cost would be prohibitive to widespread usage.

PLASMA

Although whole blood transfusions were attempted in 1818 and became frequent after Landsteiner discovered the ABO groups in 1900, plasma infusions were not widely used until 1932.[26] This is surprising as plasma fulfills most of the requirements of an ideal blood volume expander and is perhaps the most physiologically balanced colloidal solution for this use. It can be stored for long periods and can be used without crossmatching. Although 3% of the early plasma administrations were accompanied by allergic and thermal reactions[168] more recent work has emphasized the safety of plasma.[167] Serum hepatitis transmission can be prevented by storage of plasma at 76 to 96° F for 6 months. In contrast to a transmission rate of 1.9% in patients receiving blood, Allen has shown that hepatitis is not transmitted if patients receive plasma stored at room temperature for 6 months.[167, 168] Plasma is not the final answer, however, and in addition to its limited supply and high cost

there are other disadvantages. If dogs are bled and maintained at blood pressures of 40 mm Hg for one hour, infusion of plasma will be followed by a loss of 40 to 50% of the infused volume within 30 minutes. This volume loss is accompanied by an equivalent loss of plasma proteins.[169] The reactions which follow administration of plasma are similar in many respects to reactions to whole blood and have been described by Nicholson.[170] Similar reactions can be seen in the dog. Autoinfusion of a dog's own plasma will result in expansion of plasma volume comparable to the amount infused, but administration of plasma from another dog will result in only 50% of the expected expansion. There is a concomitant loss of plasma proteins during this reaction and hypotension, urticaria and marked increases in gastric acid secretion have been observed.[171] The hypotension, urticaria, edema, prolongation of bleeding time and liver congestion which accompany these infusions of plasma in dogs are lessened to some extent by anesthesia or antihistaminic drugs.[172] This reactivity to plasma infusions may indicate that the dog is extremely sensitive to alterations of the normal colloidal balance of its blood and as such would be an excellent animal in which to survey the reactivity of parenteral colloidal solutions. Occasionally rapid infusion of citrated plasma or blood may be accompanied by toxic reactions related to hypocalcemia but these are rare and can be easily avoided by the simultaneous administration of calcium.[173, 174] Fractions of the plasma proteins such as serum albumin have been used as blood volume expanders and seem to be quite useful. Their major disadvantage is that of plasma—limited availability and high cost.

MISCELLANEOUS BLOOD VOLUME EXPANDERS

The Russians seem to be especially active in the development of esoteric compounds for use as plasma substitutes. These include: (1) aminokrovin—an oxygen hydrolyzate of the residual blood clot after extraction of the serum of the erythrocytic mass after skimming off the plasma, of corpse blood or retroplacental blood; (2) polyglukin and syncol—polyglucose and dextran respectively which have been noticed to cause hemostatic defects; (3) VK-8—an heterogenous protein solution devoid of antigenic properties; (4) L103—an incomplete acid hydrolyzate of animal blood; and (5) aminol—a fermentative hydrolyzate of animal blood.[175] Cadaver blood has been used in Russia since 1927. The formed elements remain viable for 5 hours post-mortem but the danger of bacterial contamination and toxin formation prevents widespread acceptance in this country.[20] Casein digests have been used in Europe with some success but a vasoconstrictor principle probably contributes to the effect. Subsidon is a preparation of rutin developed in Germany which presumably decreases capillary permeability but is not a colloid and is probably no better than saline.[20] Gropper *et al*[20] also note that the use of okra, colloidal salts and amino acid polymers is being considered. Although these agents along with many others have the properties necessary for the expansion of blood volume, they are undoubtedly associated with a prohibitively high rate of reactions. Colloids which are similar to normal body constituents are probably the least toxic agents for parenteral use as blood volume expanders.

STARCH

Terashima[176] measured starch concentrations in blood by ethanol precipitation and acid hydrolysis following intravenous administration of soluble starch to rabbits. He found that the blood levels of starch decrease from 490 mg/100 ml 5 minutes after the injection of 1 Gm/kg to 7 mg/100 ml at 60 minutes. With glycogen 1 Gm/kg he noted a decrease from 1200 mg/100 ml at 5 minutes to 626 mg/100 ml at 1 hour, 439 mg/100 ml at 2 hours and 40 mg/100 ml at 12 hours. Excretion of glycogen in 24 hours amounted to 8% but no free sugar was found in the urine. Starch on the other hand was excreted to the extent of 5% of that infused in 20 hours and this was accompanied by the excretion of 11% as free glucose. Terashima also noted that the blood sugar level was elevated by 50 mg/100 ml following 1 Gm/kg of soluble starch and by 75 mg/100 ml following 1 Gm/kg of glycogen. The hyperglycemia persisted for about one

hour with starch and about 3 hours with glycogen.[176] This report would seem to indicate that starches are rapidly broken down when administered intravenously but that glycogen is more resistant to filtration. It also supports the concept that intravenous administration of polysaccharides can be utilized for parenteral alimentation.

Macromolecular polymers for parenteral use must be well dispersed in a colloidal solution. Intravenous injection of suspensions of ungelatinized starch in water produces pulmonary embolization and dyspnea. A recent study of the tolerance of dogs to infusions of macromolecular polymers has demonstrated that well-gelatinized starch solutions do not give rise to dyspnea or other manifestations of pulmonary embolization.[9] These gelatinized preparations are well tolerated by dogs and anaphylactoid reactions to their injection are rare. Although reactions are uncommon, histamine release is observed following injection of small doses of starch and the magnitude of this release is equivalent to that seen with dextran.[9] Injection of small doses of starch also produces thrombocytopenia which seems to be a characteristic effect of injections of all colloids.[177]

Wiedersheim[178] has investigated the use of a corn starch with a molecular weight of 81,000 hydroxyethylated to a degree of substitution of 0.6. This starch, which he calls oxyethylstarch, is more soluble in water than native corn starch and is chemically inert, partly eliminated by the kidneys and does not cause allergic reactions. Rabbits which received 100 mg/kg of the oxyethylstarch daily for 3 months exhibited no pathological changes. When used as a 4% solution it restored the blood pressure of bled cats to control levels and even appeared superior to dextran in this regard.[178]

A recent study[179] has shown that unsubstituted starch is rapidly eliminated from the circulation when administered to bled dogs. This rapid decline in blood concentration of starch is partially caused by the very high amylase activity of dog blood but this is not the predominant factor involved. Hydroxyethylation of starch to a degree of substitution of 0.6 afforded some degree of amylase resistance and this type of starch was intermediate between dextran and unsubstituted starch in its rate of elimination.

PHYSIOCHEMICAL CONSIDERATIONS OF PLASMA SUBSTITUTES

The water-binding capacity of the colloid is of greatest interest. The amount of water actually bound by the serum proteins in a layer of hydration does not exceed 0.4 ml/Gm.[180] However it has been calculated that each gram of albumin actually holds 18 ml of water in the circulation. Two-thirds of this effect (12 ml) is due to the colloidal osmotic pressure exerted by albumin. The remaining 6 ml are held intravascularly by the Donnan effect of the charge on the proteins.[181] This consideration clearly indicates the superiority of a charged polymer as compared with uncharged molecules such as dextran and starch.

Two other physical considerations are important in evaluating plasma substitutes. The colloidal osmotic pressure of the substitute should be in the same range as that of normal human serum which is 33 cm H_2O with a range of 28 to 48 cm H_2O.[180] It may be possible however to administer a more osmotically active concentrated solution in smaller volume with the expectation that fluid will be drawn into the circulatory system from the interstitial space. One of the limiting factors in the administration of colloids is their viscosity. The major hazard in administration of highly viscous solutions is the tendency to "overload" the circulation.

There has been little consideration of the development of plasma substitutes with different periods of circulatory retention for different applications. These colloids can be used in many ways: (1) to restore blood volume in oligemic shock when blood is not available, (2) to temporarily maintain a patient in shock until blood can be obtained, (3) to increase plasma volume in the hemoconcentration hypovolemia of burn shock, (4) to maintain colloidal osmotic pressure and prevent edema during cardiopulmonary bypass and the hypoproteinemia of starvation, liver disease, etc. (5) to produce tissue dehydration as in reduction of brain volume before neuro-

surgery, and (6) for parenteral alimentation. For each of these applications there is an optimum persistence of the colloid in the circulation.

The persistence of macromolecular polymers in the circulation depends upon the rate of degradation and the rate of filtration through capillary walls of the tissues and the kidney glomeruli. The molecular weight and spatial configuration of the polymer thus assume great importance and the number average molecular weight is probably more important since it corresponds more closely to osmotic pressure. The number average will change more rapidly than the weight average however since the smaller molecules will be excreted more rapidly. The range of molecular weight is also quite important as a sample with a range of 60,000 to 80,000 is grossly different from one with a range of 20,000 to 120,000.

It appears to be possible to produce starches with almost any degree of amylase resistance in any range of molecular weight distribution. If this is true it would enable development of a series of solutions with almost any "half-life" in the circulation.

Campbell[100] notes that there are so many dynamic factors involved in determining the efficiency of plasma substitutes that it is impossible to predict the behavior of these colloids from their physical characteristics. This is quite unfortunate as it necessitates animal screening of a wide variety of products and no one type of screening procedure is adequate due to the multiple applications of these colloids.

In concluding, it might be pointed out that, with these polymers, the incidence of adverse effects is generally related to the dissimilarity between their chemical structure and that of normal body constituents. Dextran, a glucose polymer related to glycogen, is now the most commonly used plasma substitute. Starch is still closer in chemical similarity to body glycogen and a study of its derivatives is under way in these laboratories.

LIST OF REFERENCES

The following is a list of the abbreviations of the journals cited in this review. Only the surname of the first author is included in this bibliography.

A	Anesthesiology
ABB	Arch. Biochem. & Biophys.
AC	Analyt. Chem.
ACS	Acta chir. scandinav.
AIM	A. M. A. Arch. Int. Med.
AIP	Arch. internat. pharmacodyn.
AJCP	Am. J. Clin. Path.
AJMS	Am. J. M. Sc.
AJPa	Am. J. Path.
AJPh	Am. J. Physiol.
AJS	Am. J. Surg.
AMS	Acta med. scandinav.
AnS	Ann. Surg.
ANYA	Ann. New York Acad. Sc.
AP	A. M. A. Arch. Path.
APF	Ann. Pharm. Franc.
APS	Acta physiol. scandinav.
AS	A. M. A. Arch. Surg.
BH	Bibl. haemat.
BJP	Brit. J. Pharmacol.
BMJ	Brit. M. J.
BR	Biol. Rev.
C	Circulation
CJBP	Canad. J. Biochem. & Physiol.
CMAJ	Canad. M. A. J.
CR	Circulation Res.
CRSB	Compt. rend. Soc. de biol.
FP	Fed. Proc.
IAS	Inter. Abstr. Surg.
JAMA	J. A. M. A.
JAP	J. Appl. Physiol.
JBC	J. Biol. Chem.
JCCP	J. Cell. & Comp. Physiol.
JCI	J. Clin. Invest.
JEM	J. Exper. Med.
JI	J. Immunol.
JJG	Jap. J. Gastroenterology
JLCM	J. Lab. & Clin. Med.
JPET	J. Pharmacol. & Exper. Therap.
JPP	J. Pharm. & Pharmacol.
L	Lancet
MADC	M. Ann. District of Columbia
MMW	München. med. Wchnschr.
N	Nature, London
NEJM	New England J. Med.
PRSM	Proc. Roy. Soc. Med.
PSEB	Proc. Soc. Exper. Biol. & Med.
QJEP	Quart. J. Exper. Physiol.
S	Surgery
SF	Surg. Forum
SGO	Surg. Gynec. & Obst.
SMB	Stanford M. Bull.
TRBM	Texas Rep. Biol. & Med.

1. Amberson BR 12:48, 1937
2. Bayliss JPET 15:29, 1920
3. Bollman AS 63:718, 1951
4. Ivy SGO 76:85, 1943
5. Studdiford SGO 64:772, 1937
6. Hanzlik AIM 36:447, 1925
7. Busquet CRSB 100:642, 1929
8. Hanzlik JPET 14:379, 1920
9. Walton JPET 127:39, 1959
10. Christie PSEB 32:670, 1935
11. Hueper AJPa 18:895, 1942
12. Hall JLCM 26:330, 1940
13. Erickson AJPa 14:537, 1938
14. Maas QJEP 28:315, 1938
15. Andersch JPET 52:390, 1934
16. Jackson JPET 65:440, 1939
17. Dick JAMA 105:654, 1935
18. Heckel JEM 67:345, 1938
19. Yuile JEM 70:605, 1939
20. Gropper IAS 95:521, 1952
21. Hueper AJS 56:629, 1942
22. Hueper AP 33:1, 1942
23. Hueper AP 33:267, 1942
24. Hueper AP 41:130, 1946

25. Hartman AnS 114:212, 1941
26. Drill *Pharmacology in Medicine* 2nd Ed. McGraw-Hill, 1958. Ch. 39.
27. Popper AS 50:34, 1945
28. Hartman AS 63:728, 1951
29. Hartman ANYA 55:504, 1952
30. Hueper AP 34:883, 1942
31. Behrmann BH 7:288, 1958
32. Hamilton AJPh 150:641, 1947
33. Strumia ANYA 55:485, 1952
34. Vars ANYA 55:496, 1952
35. Hogan JAMA 64:721, 1915
36. Hyde SGO 95:657, 1952
37. Govier ANYA 55:491, 1952
38. Levinson SGO 84:925, 1947
39. Hoffman JCI 25:575, 1946
40. Howard SGO 100:207, 1955
41. Maurer JEM 100:497, 1954
42. Maurer JEM 100:515, 1954
43. Maurer JLCM 52:733, 1958
44. Horvath JAP 7:614, 1955
45. Morehead AJPa 21:333, 1945
46. Skinsnes SGO 85:563, 1947
47. Anderson JAMA 114:1983, 1940
48. Feher S 12:705, 1942
49. Ravdin AS 63:745, 1951
50. Fletcher JCI 24:405, 1945
51. Miller JCCP 22:127, 1943
52. Knoefel JPET 83:185, 1945
53. Thorsén ACS Suppl 154:1, 1950
54. Parkins AJPh 173:403, 1953
55. Julliard BH 7:282, 1958
56. Elder BH 7:278, 1958
57. Ravdin JAMA 150:10, 1952
58. Behrmann FP 13:10, 1954
59. Campbell TRBM 9:235, 1951
60. Higgins JAP 4:776, 1952
61. Raisz AJPh 169:475, 1952
62. Feigen SMB 11:1, 1953
63. Taylor CMAJ 44:547, 1941
64. State S 22:424, 1947
65. Hecht MMW 90:11, 1943
66. Wilkinson L 1:1269, 1954
67. Valette APF 12:518, 1954
68. Thrower L 1:1096, 1951
69. Quivy AIP 105:429, 1956
70. Marshall AJPh 189:209, 1957
71. Halpern BJP 10:223, 1955
72. Narat AS 64:80, 1952
73. Loubatières CRSB 142:1340, 1948
74. Halpern CRSB 147:643, 1953
75. Perlmutt PSEB 83:146, 1953
76. Maurer JI 77:105, 1956
77. Maurer JI 79:84, 1957
78. Steele ANYA 55:479, 1952
79. Ravin NEJM 247:921, 1952
80. Weikel JPET 118:148, 1956
81. Nelson PSEB 76:765, 1951
82. Hueper AP 31:11, 1941
83. Hueper AP 28:510, 1939
84. Hueper JPET 70:201, 1940
85. Grönwall *Dextran and its use in colloidal infusion solutions* Almqvist and Wiksells, 1957
86. Goodman JBC 217:977, 1955
87. Hehre PSEB 54:240, 1943
88. Hehre JBC 163:221, 1946
89. Riddick AC 26:1149, 1954
90. Grönwall APS 7:97, 1944
91. Giebisch AJPh 178:168, 1954
92. Brewer PRSM 44:561, 1951
93. Howard AnS 143:369, 1956
94. Wasserman CR 3:594, 1955
95. Wasserman AJPh 171:218, 1952
96. Bloom PSEB 76:3, 1951
97. Wilson AJMS 223:364, 1952
98. Semple CJBP 32:670, 1954
99. Fleming JCI 36:1233, 1957
100. Bloom AS 63:739, 1951
101. Wasserman AJPh 176:104, 1954
102. Pirani JAP 8:193, 1955
103. Stamler AJPh 195:362, 1958
104. Thorsén SGO 109:43, 1959
105. Meyer SGO 94:712, 1952
106. Wise SF 8:18, 1957
107. Artz S 37:612, 1955
108. Johnston AJS 85:720, 1953
109. Rosenqvist AS 62:524, 1951
110. Amspacher AS 66:730, 1953
111. Juster AJPh 167:800, 1951
112. Gray AJPh 174:462, 1953
113. Grotte JLCM 38:577, 1951
114. Tarrow A 14:359, 1953
115. Johnston AJS 85:713, 1953
116. Tarrow A 16:598, 1955
117. Maycock BH 7:272, 1958
118. Young CMAJ 75:562, 1956
119. Wilkinson L 2:956, 1953
120. Henley MADC 27:21, 1958
121. Turner SGO 88:661, 1949
122. Kabat JCI 36:1160, 1957
123. Thorsén Cited Ref. 116
124. Masson AJPh 195:407, 1958
125. Marshall PSEB 97:587, 1958
126. Haining BJP 10:87, 1955
127. Sugg JI 43:119, 1942
128. Zozaya JEM 55:353, 1932
129. Neill PSEB 78:537, 1951
130. Evans JEM 74:511, 1941
131. Kabat JI 70:514, 1953
132. Hehre ANYA 55:467, 1952
133. Kabat ANYA 55:471, 1952
134. Kabat ABB 78:306, 1958
135. Carbone PSEB 90:68, 1955
136. Morrison QJEP 41:51, 1956
137. Semple JLCM 45:61, 1955 .
138. Ricketts N 169:970, 1952
139. Fletcher N 170:319, 1952
140. Marston L 2:688, 1954
141. Wallace L 2:761, 1954
142. Bowley L 2:1080, 1954
143. Waud JPET 119:85, 1957
144. Swank JAP 12:125, 1958
145. Swank JAP 10:45, 1957
146. Hardwicke PRSM 44:559, 1951
147. Hardwicke N 166:988, 1950
148. Ross JCI 38:155, 1959
149. Weil SF 6:88, 1955
150. Carbone PSEB 85:101, 1954
151. Jaenike C 11:1, 1955
152. Adelson BH 7:275, 1958
153. Semple AJPh 176:113, 1954
154. Adelson JLCM 45:441, 1955
155. Seegers JAP 7:617, 1955
156. Jacobaeus AMS Suppl 322:1, 1957
157. Goldenberg AJCP 17:939, 1947
158. Mowry JLCM 39:211, 1952
159. Mowry AJPa 29:523, 1953
160. Vickery AJPa 32:161, 1956
161. Terry JLCM 42:6, 1953
162. Gray PSEB 77:626, 1951
163. Cargill JPET 103:339, 1951
164. Howard AJS 97:593, 1959
165. Harrison AnS 142:824, 1955
166. Miller JAMA 128:863, 1945
167. Sayman JAMA 168:1735, 1958
168. Allen SGO 100:495, 1955
169. Wasserman FP 11:168, 1952
170. Nicholson A 9:345, 1948
171. Bliss CR 7:79, 1959
172. Remington AJPh 197:193, 1959
173. Bruneau AS 47:319, 1943

174. Ludbrook BMJ 2:523, 1958
175. Bogomolova BMJ 2:354, 1956
176. Terashima JJG 9:273, 1937
177. Bloom AMS 162:423, 1958
178. Wiedersheim AIP 111:353, 1957
179. Thompson FP 19:103, 1960
180. Campbell JPP 8:93, 1956
181. Scatchard JCI 23:458, 1944

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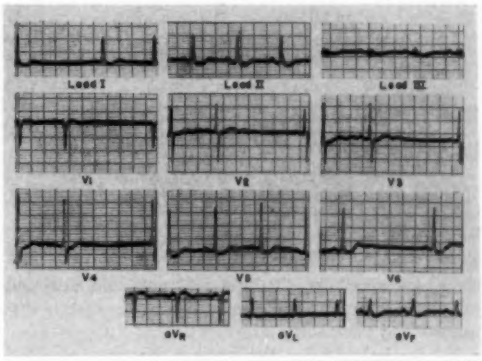
ELECTROCARDIOGRAM OF THE MONTH

Sino-atrial block

DALE GROOM, M. D.
Department of Medicine



Case Record—This electrocardiogram was made at rest on a 71-year-old lady with a history of typical angina pectoris of about eight months duration. During that time she had been treated with digitalis and diuretics, apparently with some improvement in her dyspnea and occasional ankle edema. Her past medical history was notable only for questionable chorea in childhood and removal of both ovaries in early adult life.

Her major complaint at this examination was that of an irregularity of her pulse. For several weeks she had been aware of a sensation of her heart stopping intermittently, associated with transient giddiness, then a disturbing and very forceful beat. These symptoms were thought to have been present prior to digitalization.

Electrocardiogram—Aside from a minimal sinus arrhythmia, the rhythm is basically a regular one at a rate of 90 which is punctuated by discrete pauses. These pauses during which time there is no sign of atrial activity are approximately double the regular cycle length in all instances. Long strips of tracing disclosed no constant sequence of repetition of the pauses, they occurring every minute or so at the time this electrocardiogram was made.

Careful measurement of the P-R intervals shows that they do vary slightly and in a repetitive pattern; always a little shorter (0.14) on the beat immediately following the pauses than on all other beats where they are 0.16 in length. Normal contour of the P waves throughout denotes their uniform origin from the sino-atrial node.

Additionally there are S-T depressions of 1 mm. in V_4 and V_5, some T wave changes consistent with digitalis effect, and conspicuous U waves in several leads.

Discussion—Such momentary and usually recurrent interruptions of atrial activation have been divided into ***sinus arrest***[1] in which the pauses are due to momentary failure of the SA node to initiate impulses, and ***sino-atrial block*** ascribed to intermittent failure of conduction of the normal impulses from the pacemaker node to the atria. In the latter case the pauses are necessarily multiples of the regular cycle length, as contrasted with the periods of sinus arrest which are of random length. Both produce similar symptoms the severity of which depend in large part upon the duration of the periods of asystole. A unique characteristic of sino-atrial block is the occasional doubling or halving of the rate abruptly which is reported to take place with an intermittent (2:1) block of every alternate impulse.

Presumably a boundary exists across which the impulse must go from the SA node to the atrial muscle. If the threshold of the boundary is such that an occasional beat fails to leave the node, a dropped beat results in an otherwise regular rhythm. Quite possibly this phenomenon is analogous to the Wenckebach intervals of AV block, the threshold progressively rising to a critical level at which the impulse cannot escape from the pacemaking node, followed by a pause and then enhancement of conduction (note the shorter P-R intervals after each omission of a cycle). Whatever the mechanisms involved, sino-atrial block is considered by some to be more indicative of myocardial disease than simple sinus arrest which oftentimes amounts to little more than another variation (e.g., sinus arrhythmia, tachycardia, bradycardia, etc.) in the rate of impulse formation. However it should be noted that very long and doubtless sometimes fatal periods of asystole can occur with the sinus arrest caused by, for example, carotid sinus stimulation. The possible role of autonomic innervation in both types of atrial standstill is suggested by the frequent association of sinus arrhythmia with them. Electrolyte disorders, myocarditis and certain drugs, notably digitalis, have also been implicated. In this patient, with angina pectoris and S-T depressions consistent with ischemia, one might postulate a causal relationship between her coronary insufficiency and the sino-atrial block.

It is worthy of mention that the chief symptoms arising from brief interruptions in cardiac activity almost always pertain to the beat following the pause. This holds true in the common extrasystoles, in sinus pauses and, frequently, in atrial fibrillation. A reasonable explanation is that the familiar thump in the

chest is caused by an unusually forceful beat with a high stroke volume resulting from the prolonged period of ventricular filling.

REFERENCE

1. Groom, Dale; Sinus arrest, J. South Carolina M. A., April, 1959.

ACKNOWLEDGEMENT

I am indebted to Dr. Cheves Smythe of the Medical College of S. C. for submitting this interesting case.

POSTOPERATIVE COMPLICATIONS—III. ABDOMINAL WOUND DISRUPTION

R. Randolph Bradham, M. D.

Department of Surgery

W. J. W. was an 81 year old white male admitted to the Medical College Hospital on June 4, 1960 with the chief complaint of abdominal pain and vomiting of 9 days duration. The abdomen was moderately distended and tympanitic especially in the upper quadrants. It appeared that the stomach was markedly distended. An upper gastrointestinal series on June 7 revealed moderate gastric outlet obstruction believed to be secondary to a benign process. The stomach was decompressed with continuous suction. Following this, milk in 200 ml. amounts was given and followed by aspiration of the stomach several hours later. This was continued for 3 days but repeatedly the amount aspirated was greater than the amount instilled. At the end of 6 days of conservative therapy, decision was made to relieve the obstruction by operation. A gastrojejunostomy combined with vagotomy was elected rather than subtotal gastrectomy as it was believed that the process was benign and that in the patient's weakened condition, the proposed procedure would be better tolerated.

This procedure was done on June 11. The obstruction was due to a cicatrix caused by an old peptic ulcer process. Oral fluids were given beginning on June 15. The following day there was moderate abdominal distention and hypoactive peristalsis. A moderate, persistent cough developed postoperatively. A roentgenogram of the abdomen with the patient in the supine position revealed reflex ileus. A lateral roentgenogram with the patient in the same position revealed gas filled small bowel extending to near the skin line. Because there appeared to be a small amount of fluid beneath the skin, the wound was examined. The anterior rectus sheath was found to be disrupted and a probe passed into the peritoneal cavity. Preparation was begun for operation immediately. At operation, it was found that the lower half of the operative wound was completely disrupted except for the skin. The anterior rectus sheath in the upper one half of the wound was also disrupted but the posterior sheath was intact. There was moderate distention of the stomach, small, and large bowel. A decompressing enterostomy was necessary. The abdomen was closed with large stainless steel wire retention sutures placed through the full thickness of the abdominal wall. The patient had a relatively stormy postoperative course but eventually recovered.

Discussion

Incomplete wound disruptions often go unrecognized only to become manifest later as ventral hernias. The more serious wound disruptions are those in which the wound edges separate completely and the abdominal organs eviscerate. This occurrence in an elderly patient with a serious illness carries a high mortality, quoted anywhere from 20 to 70% in papers on this subject. The incidence of this complication has decreased with the numerous advances in surgical technique, antibiotics and supportive care.

Malnutrition, hypoproteinemia, chronic anemia, vitamin C deficiency, and constitutional disease predispose to wound disruption. Hypoproteinemia and vitamin C deficiency experimentally and clinically have been found to delay wound healing. All of these factors are rather difficult to assess. Many patients are operated upon with one or more of these factors existing at the time of operation and have no wound complication. Other patients experience wound disruption yet are known to have none of these predisposing factors. Certainly the patient who is in poor condition prior to, during, or following an operation will be more prone to poor wound healing. All factors predisposing to wound disruption should be corrected as well as possible, prior to operation.

Improper selection of suture material, defective suture technique, careless hemostasis, the occasional idiosyncrasey to absorbable material will compromise the competency of the wound. Wound disruptions occur, however, with every type of suture material and method of closure making it difficult to draw any conclusions as to the preferred suture material and technique of closing wounds.[1, 2] Most clinics prefer a non-absorbable suture that causes minimal tissue reaction. When fascial layers are closed with interrupted stainless steel wire sutures, the wound is given maximum security.

Opinion in the literature is divided concerning infection in wounds predisposing to wound disruption. In one group of patients with this complication, 20 of 33 had wound infections,[3] and in another group of 113 patients, 35% had a febrile postoperative course and 13% had a frank wound infection.[2]

What part drains and ostomies play in producing wound disruption has also been difficult to assess. Most investigators, however, have advised bringing drains and ostomies out through separate wounds.[2-4] Evisceration of a wound incision with a colostomy is certainly more difficult to handle than evisceration without a colostomy.

Wound disruptions occur in every type of incision. Hartzell and Winfield[5] in their collective review of 1,458 cases of wound disruption found that the greater number occurred in upper abdominal vertical incisions, particularly in the muscle-splitting type. In the majority of the surveys, this was the incision most commonly used, therefore, the most likely to disrupt on the basis of its most frequent use. In the upper

abdomen, the transverse incision preserves the nerve and blood supply, preserves the transversalis muscle, and gives a better purchase for sutures in the fascia with its transverse fibers. The lateral pull of the transverse and oblique muscles of the abdominal wall is avoided. It would seem to be the preferable incision to use in this location.

There is overall agreement that an increase in intra-abdominal pressure is the most important single factor relative to wound disruption. Retching, persistent coughing, unrelieved hiccoughs, habitual sneezing and distention are prime factors in disrupting even the most carefully closed wound. One or more of these factors occurring to an excessive degree was found in 75% of the cases reported by Tweedie and Long[2] and in 50% of those reported by Hartzell and Winfield.[3] Every effort should be made to present and clear up any factor causing increased intra-abdominal pressure.

Suspicion that subcutaneous wound disruption has occurred warrants careful investigation of the incision, even to the extent of removing skin sutures to allow examination of the fascial layers. Intestinal obstruction, palpation of a loop of bowel under the skin, severe localized pain, and shock should dictate close scrutiny of the wound. Sudden, profuse, pink, serous drainage from a previously dry wound is virtually pathognomonic of wound disruption.

Once the diagnosis has been established, the patient should be intubated, and treated for shock should it exist. If an evisceration has occurred, the extruded viscera should be covered with sterile towels. With good relaxing anesthesia, viscera can be replaced and the wound can be secondarily closed with large retention sutures. Suture of the individual layers is often possible also.

Our patient exhibited many of the factors predisposing to and causing wound disruption. His body proteins and vitamin C levels were undoubtedly diminished during the 16 day period of relative starvation while he was obstructed. The postoperative cough and abdominal distention, although of short duration, were enough to increase his intra-abdominal pressure sufficiently to disrupt the wound. Fortunately, this was suspected and investigated early and the catastrophe of evisceration was aborted. In hindsight, this patient was an excellent candidate for retention sutures placed through the full thickness of the abdominal wall at the first operation. Retention sutures should be used prophylactically in such depleted patients.

REFERENCES

1. Sedgwick, C. E., Sullivan, J. T., Jr.: Abdominal wound disruptions: analysis of 217 cases. S. Clin. North America. 37:731, 1957.
2. Tweedie, F. J., Long, R. C.: Abdominal wound disruption. Surg. Gynec. & Obst. 99:41, 1954.
3. Hartzell, J. B., Winfield, J. M.: Disruption of abdominal wounds: Collective Review. Internat. Abstr. Surg. 68:585, 1939.
4. Mersheimer, W. L., Winfield, J. M.: Abdominal wound disruption: a review of the etiology, recognition and management. S. Clin. North America. 35:471, 1955.

The presence of the artificial kidney at the Medical College Hospital and the activation of the Saul Alexander Research Unit has resulted in the referral of a number of patients with a wide variety of renal diseases to the Medical College Hospital. The editors of *The Journal* are instituting this series of clinics on medical aspects of various kidney diseases with the idea that some of the value of this concentration of experience might be shared with the readers of *The Journal.*

RENAL DISEASE

Azotemia secondary to electrolyte depletion induced by diuretics

CHEVES MCC. SMYTHE, M. D. & ROY HOWELL, M. D.
Department of Medicine

Enthusiastic use of the mercurial diuretics 15 years ago resulted in electrolyte depletion and azotemia on which attention was focused by Schroeder's paper on the low salt syndrome. The introduction and extensive use of the chlorthiazides in many clinical states has created clinical syndromes secondary to their potent effect on sodium, chloride and potassium excretion.

JMS, #25197, a 35 year old Negro male, was referred to the Medical College Hospital because of acutely progressive renal failure with oliguria.

The present illness began in 1943, 16 years before his admission to the hospital, with his rejection by the draft board for hypertension.

At the end of June, 1959, 6 weeks before his admission to the Medical College Hospital, while working in his fields on a hot day, he suddenly became dizzy and weak. His left arm became weak and numb. At the same time, he became short of breath and was unable to lie flat in bed. He lay at home for about 3 weeks and then was admitted to his county hospital on July 16, 1959. He was afebrile, had a sinus tachycardia of 120, and a blood pressure of 180/30 mm. Hg. He was a well developed, well nourished, chronically ill Negro man. His speech was slightly slurred, and he was not entirely clear mentally.

The eyegrounds revealed arteriolar narrowing with silver wire appearance of the arterioles. There was also nicking of the veins at the arteriolar venous crossings which is indicative of thickening of the arteriolar wall and chronicity of the hypertension. No hemorrhages or exudates were noted and there was no papilledema. The heart was enlarged 2 cm. to the left of the midclavicular line in the sixth intercostal space. Multiple premature ventricular contractions were heard. There were a few fine rales at both lung bases. There was minimal pretibial edema.

There was weakness of the left arm. No pathological reflexes were noted and no other neurological abnormalities were described.

His urine concentrated to 1.013 and contained a

trace of albumin. His white count was 24,000/cu. mm. with 90% polymorphonuclears. A blood non-protein nitrogen was 67 mg./100 ml. Phenosulphonphthalin excretion was 69% in two hours. Urine culture was negative. An electrocardiogram was consistent with left ventricular hypertrophy. A chest film showed left ventricular hypertrophy. Intravenous pyelograms were normal.

On admission to the hospital he was digitalized and given 2 ml. of Mercuhydrin. He was also started on chlorothiazide, 0.5 Gm. daily, Raudixin (Rauwolfia) 100 mg. daily, and a mixture of potassium salts containing 30 mEq daily. Seventy-two hours later he was feeling considerably better. His nausea had subsided and his mental condition cleared up. His blood pressure had fallen to 140/85. The blood non-protein nitrogen which had been 67 mg. or slightly elevated, fell to 39.5 mg. Despite these evidences of improvement, by his fifth hospital day the patient seemed to become weaker. His blood pressure remained in the neighborhood of 120/86. He then developed nausea and became apathetic, lethargic and weak. Two weeks after his admission to the hospital, he was not doing at all well. It was thought that this syndrome was due to sodium depletion and the chlorothiazide was discontinued. He next developed epigastric pain and flank pain with anorexia and nausea and vomiting. His blood pressure rose to 150/120. There were no objective findings in the abdomen. A lumbar puncture was negative. He then developed severe hiccups and increasing lethargy. He was transferred to the Medical College Hospital on August 5, 1959. His blood pressure at that time was 110/90.

His past history was not remarkable save for hypertension. He had no primary renal disease.

On physical examination on admission to the Medical College Hospital on August 5 he was a well developed, well nourished, slightly obtunded young Negro male in some distress from hiccups. His temperature was 99.8°F., pulse 95, respiration 24, and blood pressure 108/86. He weighed 162 pounds.

Physical examination was as previously described.

The initial impression was that this man had essential hypertension with a small infarct in his right cerebral hemisphere. His major problem seemed to be salt depletion secondary to the administration of chlorothiazide and sweating.

During his first night in the hospital he was given 2,000 ml. of 5% dextrose in normal saline intravenously. He was started on a 20 Gm. protein diet supplemented by 4 Gm. of sodium chloride per day orally. Hiccups were a severe problem, and he was given 25 mg. of Sparine (phenothiazine) by mouth four times daily for this and 5% CO_2 inhalations as needed. He was maintained on 0.1 Gm. of digitalis daily.

The initial urine concentrated to 1.009 and contained a trace of albumin and was otherwise clear. After he had received 2,000 ml. of normal saline or 18 Gm. of salt intravenously, his blood urea nitrogen was 28 mg., and his serum creatine was 4.6 mg. His serum chlorides were 94.6 m Eq./liter and serum sodium 130.5 m Eq./liter. CO_2 combining power was normal at 60 vol. %, and the serum potassium was 4.72 m Eq./liter. On his admission to the hospital an electrocardiogram was remarkable only for premature ventricular contractions.

On his first day in the hospital his urinary output was 1400 ml. Thereafter, the urinary output remained satisfactory. His weight remained stable at 162 pounds. On institution of salt therapy, his blood pressure rose to the neighborhood of 130/90.

Over the next 4 or 5 days in the hospital, his mental state cleared. He regained body strength, his appetite increased, his hiccups subsided, and he generally felt much better. On his third hospital day, a kidney biopsy was done (Fig. 1) This showed hyalinization of the glomeruli, hyalinization of the arteries, with reduplication of the elastica, reduction in the size and lumens of the arterioles as well as some interstitial fibrosis. The section was consistent with arteriolar nephrosclerosis without malignant change.

At the end of 6 days in the hospital the patient was feeling well and was discharged.

Discussion

The clinical picture presented by this man is that of salt depletion. This was recognized by his physician and his referral to the Medical College Hospital was suggested because of better facilities for laboratory control of his condition.

There were probably two or three factors contributing to his salt depletion. First, he became ill while working in the sun. Secondly, he lay at home partially obtunded without anyone to care for him (his wife is in a mental hospital) for about two weeks. Presumably, he was sweating. On admission to the hospital he was given chlorothiazide. The outstanding characteristic of this diuretic is that it is extremely effective in potentiating the loss of sodium and chloride with subsequent loss of water by the distal and collecting tubules. Most individuals will not deplete themselves to a clinically hyponatremic state, but those with renal disease or extrarenal losses of salt will often do so.[2] The value of chlorothiazide as an antihypertensive agent lies in its ability to deplete body sodium stores with resultant decreased volume of blood in the arteriolar tree or changes in arteriolar vessel wall tone which are eventually followed by decreases in peripheral resistance and therefore, decreased blood pressure.

The clinical picture of low body sodium was first described by O'Shaughnessy[3] during a London cholera epidemic in 1831. Recently, attention has been refocused on it under the name of the "low salt syndrome" by Schroeder.[1] Apathy, weakness, lethargy, progressing to stupor, abdominal discomfort with distention, occasional nausea and vomiting, decreased urinary output, and rising blood urea nitrogen constitutes the syndrome. In a carefully controlled study of subjects with renal disease, Nickel, *et al*[4] demonstrated that depleting the body of sodium was ac-

companied by a decreased renal plasma flow, decreased glomerular filtration rate, and rising blood urea nitrogen. Repletion of these patient's sodium was attended by a return of all of these physiological parameters to normal.

Therefore, in the presence of renal disease or other conditions which cause an excessive drain of sodium from the body, the chlorothiazides should be administered to patients carefully. Their use is not contraindicated, but especially during the early stages of its administration, the patients should be followed carefully with the idea in mind that unexpected symptoms might be due to excessive sodium or potassium losses. Weakness is characteristically the first of these.

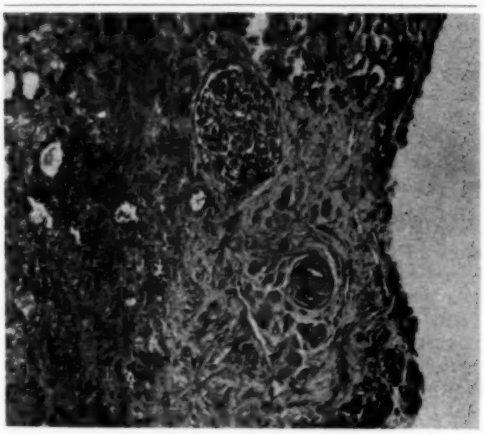


Fig. 1 x 150. Arteriolar nephrosclerosis. The small arteriole with its greatly thickened wall is the most striking change. This thickening is largely of the subintimal layers of the media. In addition, a lamellar change of the adventitia is apparent. There is an increased amount of fibrous interstitial tissue surrounding the arteriole. The glomerulus is not remarkable.

The treatment of this condition is by sodium chloride. This can be given either intravenously or as salt tablets by mouth. Characteristically, these patients respond slowly and three or four days must go by before they are feeling well again. Careful calculation of the dosage of sodium chloride is not important in patients who are relatively well. In a patient such as this, the administration of 4 to 6 Gm. of sodium chloride in addition to what is taken orally will replete him at a satisfactory rate. This is usually given after a loading dose of 18 to 27 Gm. of salt.

The kidney biopsy in this patient revealed that his renal histology was completely consistent with hypertension as the etiology of his renal disease. There are no other conditions suggested and the illustration is quite typical of nephrosclerosis.

This man is now doing well. He has gained 30 pounds and is working full time with fair control of his hypertension with antihypertensive agents.

REFERENCES

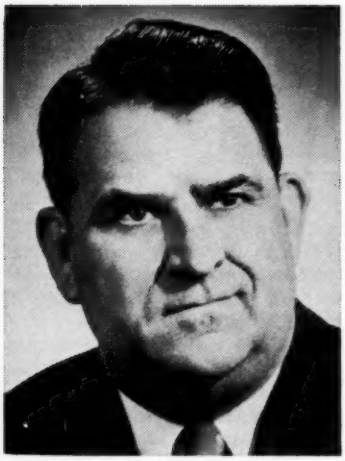
1. Schroeder, H. A.: Renal failure associated with low extracellular sodium chloride; the low salt syndrome. J.A.M.A. 141: 117, 1949.
2. Fuchs, M., Mallin, S. R., Irie, S., Hernando, L., and Moyer, J. H.: A review of the pharmacology and clinical observations of hydrochlorothiazide. A.M.A. Arch. Int. Med. 105: 39, 1960.
3. O'Shaughnessy, W. B.: Experiments on the blood in cholera. Lancet 1: 490, 1831-32.
4. Nickel, J. F., Lowrance, P. B., Leifer, E., and Bradley, S. E.: Renal function, electrolyte excretion and body fluids in patients with chronic renal insufficiency before and after sodium deprivation. J. Clin. Invest. 32: 68, 1953.

A survey of the various attitudes in the relationship between psychiatry and religion. Norton Williams (Charleston) South. M. J. 973 (Aug.) 1960.

The purpose of this article was to survey the various attitudes and feelings that at present exist about the relationship between psychiatry and religion. The rapid growth of psychiatric theories and techniques has brought about an awareness on the part of many ministers that character change and character development are an integral part of psychiatric practice today. Mere symptom removal, although a very important part of the psychiatric work, is more clearly seen today as not a sufficiently high goal to be considered the full range of psychiatric work. This, of course, places psychiatric work astride the entire field of religion.

To those working ultimately and scrupulously in the fields of psychotherapy and psychoanalysis, the tremendous importance of some work with character change and development is obvious. This paper, therefore, is devoted to an attempt to delineate the role of both psychiatry and religion in this important phase of professional effort. The basic idea advanced is the part that organized religion can play in forming a setting that can substantiate and elaborate in everyday living what the psychotherapist or analyst does in the structural setting of his office work with the patient.

It is hoped that much further cooperative effort will continue in this new and growing field between psychiatry and religion.



President's Pages

Last month's President's Pages contained my remarks to the students of the Medical College on its opening day. The local newspapers printed portions of these remarks at the time and one of them commented editorially. A resume was sent out over the Associated Press and was published in several papers over the state. The publicity given these remarks emphasized the statements concerning high fees and socialized medicine and has caused certain reactions among those who read them. It is these reactions which prompt further comment from me this month concerning medical fees in particular.

First, came the comments from the doctors, some of whom resented the papers taking out of context the part pertaining to high medical fees and playing it up. They felt that the newspapers and the public themselves were not in a position to know what a high medical fee really was. Some felt that their fees were not high, particularly when taken in relation to charges by television repairmen, air-conditioning and heating contractors, plumbers, auto repairmen, and other trade technicians. Some were confident that their net income this year has been lower than it was five years ago, even though their gross might possibly be higher. High rentals and materials, increased wages and shorter hours for help, etc., has greatly increased their overhead.

These contentions have a great deal of merit.

Most medical fees are not out of line when compared with charges by people representing other vocations, when time required and expenses incurred for proper training is brought into its true perspective.

Most doctors do not overcharge. Undoubtedly, some do.

However, medical charges when combined with the increasing cost of drugs and hospitalization, whose charges seem to be in a continuous spiral, often reach a peak which spells catastrophe for many people.

Add to this existent evidence that indicates some few doctors do overcharge in fact, and that at times others will present bills which appear on the face to be out of line, and we have a situation ready made to create a feeling of intolerance toward all medical fees, with the doctor in the middle. Since he prescribes the medicine and orders the hospitalization the entire blame is often put on him. That this is so, is verified by the reaction of the general public to the newspaper publicity spoken of above.

Since that time I have traveled around the state, and have been amazed at the number of lay people who have sought me out at various meetings and told me how much they agreed with what the papers said. So many in fact, that I was convinced I should write on the same subject this month. All the doctors in our Association should know that the public is keenly cognizant of the high cost of medical care, and that they blame it on the doctors. Whether this is justified, or whether it is not, has no bearing on their attitude.

Herein lies the crux of the problem.

The public does not understand all the various facets involved, and we HAVE NOT TAKEN THE TROUBLE TO DISCUSS THESE WITH THEM. There are a few people who are down on doctors along with everything else, and who will not listen to logic no matter how presented. However, the vast proportion of people are fair minded and will listen. It is up to us to persuade them that we are not greedy ogres who would keep them from getting proper medical care because of exorbitant cost, as many would have us believe.

In its public relations program, our Medical Association already has tried to present cer-

tain of these facts to the public through the newspapers, radio, and television. However much more needs to be done.

The public needs to be educated that medical expenses, even if they are high, can usually be insured against. We should not only let them know that insurance is available, but we should actively discuss the problem of prepaid medical care so that they might get all of the available information about Blue Cross and Blue Shield, and other reliable insurance plans that come to our attention.

I think that it would be in order for each physician to have in his outer office a sign which would state something like this:

"Are you adequately insured against medical expenses? This office will be glad to advise and consult with you concerning your insurance if you so desire."

A little interest on our part in our patients being properly insured will help them select adequate coverage and avoid keen disappointment after becoming ill when their policy does not cover their particular ailment, or has such small benefits as to be of practically no help.

We should make it a policy of discussing our fees with our patients before hand so that they will know approximately what to expect. If the service that they are to receive is of a particularly specialized nature, this should be explained also.

If they have insurance it should be understood in advance whether this insurance will be accepted as payment in full, or if additional payment will be necessary.

Those of us who use the patient's financial level as the yardstick as to what he will be charged, should be sure that the patient understands this way of thinking. Otherwise, discontent will arise because of different bills to patients for similar service. This usually comes out in the "gab fest" after the operation or illness, when one patient is trying to "out brag" the other.

I would recommend that each of us start a public relations campaign of our own, individually in our own office on our own patients. This should grow into an educational project at the local level, involving the Hospital Staff or County Society. We should let the people know the true facts concerning medical fees.

To help with this campaign I submit the following for your study. This article has also been sent to Mr. Tom Waring, Editor of the News and Courier.

This was in reply to a nationally syndicated column, appearing regularly in the Charlotte Observer, a financial column by Sylvia Porter. She wrote an article assailing the high cost of medical care and stated that it had increased during the past few years far above the normal increase in the cost of living. As a result of this article, a committee of physicians in Charlotte wrote to the paper and asked for permission to submit an article in rebuttal. The article follows:

In her column, dated January 12, entitled "Medical Costs Shocking" Sylvia Porter cited figures, apparently taken from context, which are incomplete.

When used in this manner they create an impression which is at times inaccurate and distorted. It is our desire to rectify some of the omissions — particularly with reference to physicians' fees.

The truth is, medical and hospital services — although they are unique in that they involve the lives and health of human beings — are nevertheless subject to the same economic pressures as other services and commodities.

They are not completely apart from the laws and workings of a free economy.

Concern over medical cost, if it is to be reasonable and logical, should be just one part of an overall concern regarding the inflationary trend of our entire economy.

This trend began around 1939 or 1940 and is continuing to this day. True, within that framework, hospital and other medical costs have risen.

The important question is how far and how fast have they gone up — in relation to the American people's income, purchasing power, and payments for other services and commodities?

According to the United States Department of Commerce, personal consumption ex-

penditures (this does not include public or governmental spending) totaled some 267 billion dollars in 1956.

Of this amount 32 per cent went for food and tobacco; 10.1 per cent for clothing and jewelry; 12 per cent for housing; 11.3 per cent for transportation. Only 4.5 went for total medical care. This includes physicians' services, hospitals, dentists' services, drugs and sundries, health insurance, and miscellaneous services, products and appliances.

When we examine the base period of 1935-1939, we find that the American people spent 4.1 per cent of all their personal expenditures on medical care. So percentage-wise, from that period to 1956, the increase was from 4.1 to 4.5 per cent.

In 1956 the 4.5 per cent of personal consumption expenditures which went for total medical care was divided up as follows: For physicians 1.22 per cent; for hospitals, 1.3 per cent; for drugs and sundries, 0.7 per cent; for dentists, 0.4 per cent; for all other, 0.9.

In 1955, the American people spent over $13 billion on recreation — almost $2 billion more than they did on all medical care that year.

They spent over $9 billion on alcoholic beverages; this is almost 50 per cent more on alcohol than on physicians and hospitals combined.

They spent almost as much on tobacco as on physicians and hospitals together.

And they spent more on personal care — that is, toilet articles, barber shops, beauty parlors, and the like — than they did on either physicians or hospitals, taken separately.

These relationships between medical care and less essential commodities and services have existed for the past 25 years; together with the steady ratio between medical expenditures and all other consumer expenditures, they indicate a stability which could not exist if supply and demand were seriously out of balance in the field of medical services, or if the people had been subjected to excessive price rises.

Now, let's examine the behavior of medical prices.

Miss Porter states in her column that "general practitioners' fees have climbed 39 per cent . . . surgeon's fees have risen 26 per cent."

She also states that the cost of medical care has risen far more than the overall cost of living and that only the pace of the rise in transportation costs have topped the pace in the rise of medical expenses.

She continues, "the cost of medical care has gone up much more than the cost of food, housing, apparel, etc."

Concerning the fees of general practitioners and surgeons, our information (from the U. S. Bureau of Labor Statistics) shows that these fees lagged far behind the rise of the Consumer Price Index up until 1954.

The discrepancy is explained if Miss Porter used 1949-50 as her base period (160) rather than 1940.

Charts purporting to show that the cost of medical care has risen higher than the cost of living in the last decade appear, on closer scrutiny, to be something of an optical illusion.

In the 1950-57 chart, physicians' fees and medical care and drugs apparently rose higher than the consumer price index, taking the base period as 1947-49.

But the 1940-57 chart shows exactly the reverse: physicians' fees and medical costs are below the consumer index. (Using a base rate 1935-1939-100). Both charts show generally higher hospital costs.

It has also been calculated that 11 office calls cost a production worker a sum equal to one week's wages in 1935-39; in 1957 the same number of calls would have cost him only 49 per cent of one week's wages.

A recent study of the 1936-56 span published by the U. S. Bureau of Labor Statistics said: " . . . the price increase over the 20-year period was smaller for medical care other than hospitalization than for any one of the major groups."

It appears to us that physicians have followed rather than led in the rising price index.

Another way to gain perspective on the problem of medical costs is to look at the distribution of the medical dollar.

Ever since 1945 the percentage going for physicians' services has been declining, and the percentage going to hospitals has been increasing. Finally, in 1955, the hospitals' share passed the physicians' portion — 27.8 per cent for hospitals and 27.2 per cent for physicians. But the two together still make up only 55 per cent of all medical expenditures.

Drugs and sundries take 15.5 per cent; dentists' services nine per cent.

A fifth category — including such things as eyeglasses, orthopedic appliances, osteopaths and health insurance overhead costs — takes up 20.5 per cent.

This suggests that the question of controlling medical costs is not one problem but several — and with many subdivisions.

Moreover, it focuses attention on the fact that the major problem is hospital costs — not through any fault of the hospitals themselves, but rather because hospitals are being used more and more, because they are especially vulnerable to rising overhead costs, and because their price rises already have been much higher than average.

Still another factor in the picture is the distribution of medical expenses.

A 1953 survey by the Health Information Foundation showed that eight per cent of American families had no medical costs.

The vast majority of Americans in any year incur moderate medical expenses, but the distribution is uncertain.

A small proportion of individuals or families — either through one long, severe illness or because of a succession of illnesses — may encounter financial hardship, especially if they have been unwilling or unable to protect themselves by budgeting or by insurance.

To meet this problem of spotty, uneven distribution of medical expenses, the American people — as free agents in a free society — have adopted the mechanism of voluntary health insurance. Its growth and development over the past 25 years, and especially during the postwar years, have provided one of the brightest chapters in our economic history.

At the end of 1956, 112 million people had hospital insurance; 96 million were protected on surgical fees, and 63 million had medical fee coverage.

Most remarkable of all was the fact that in just the past five years the number of people with major medical expense coverage has increased one hundred times over — from 100,000 at the end of 1956.

Now a major insurance carrier is offering health insurance to persons over 65 years of age.

Recently the House of Delegates of the American Medical Association recommended to its members that they reduce fees for older people who have less than normal economic means.

We physicians are just as concerned about medical costs as anyone else, and we want to do all we can to keep them reasonable.

In medicine, every patient and every case is different. The patient is buying not only skill and knowledge, but also judgment, sympathy and understanding. You can't put a price tag on such things.

We appreciate very much the continued confidence of the people — our patients — and we renew our pledge to render the highest type service to them at reasonable cost.

When economic charges are leveled against us, however, we believe in all fairness that the full story, and not just part of it should be told.

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I hope that all of us can take time to study the above article and fully digest all of its contents. Besides being very interesting, it is the most concise and informative article on this subject that I have run across. I believe the entire medical profession owes a debt of gratitude to Dr. David G. Welton, Dr. Paul G. Donner, and Dr. James E. Hemphill, of Charlotte, who prepared this article and had it published in their local paper.

Joseph P. Cain, Jr., M. D.

Editorials

NATIONAL MEDICAL ASSOCIATION

This *Journal* has never undertaken to comment on the matter of race relations, feeling that it was somewhat out of its province. Our Association opened its membership to Negro physicians some years ago, or at least certain component societies have included Negro physicians, and properly so. It may be that they would like to offer some comment on the subject that we mention here.

At a recent meeting of The National Medical Association (Negro) the organization went on record as supporting Forand-type "federal legislation . . . for medical care of the aged and aging." This was done largely at the instigation of its retiring president, and it appears that the incoming president is very much opposed to the stand taken. However, the proceedings are a matter of record, and until there is some denial, it must be assumed that the vote represents the majority opinion of the membership.

The American Medical Association has been so wholeheartedly opposed to Forand-type legislation, that it seems most undesirable that a segment of the physicians of the country should take officially and definitely a stand toward the opposite direction. It might be easily inferred that a persuasive orator might have swayed the Association into doing something which he interpreted as beneficial to the group of Negro physicians. It seems unfortunate that this splitting of sentiment should come at a time which seems very crucial in decision on such matters, for certainly the recent efforts now in abeyance by virtue of adjournment of Congress will be renewed later despite the substitute legislation which was passed.

While this action of the National Medical Association may be a blow for the benefit of the Negro in some fashion, it certainly is not to be considered as any assistance in the fight which a vast majority of physicians of the country are making to preserve the personal relationship between doctor and patient and to avoid undesirable governmental control.

JOURNAL OFFICE LACKS OLD NUMBERS

With the various changes of editors and offices over the past years it seems that it has not been possible to maintain a complete file of this Journal, and the editor would like to appeal to anyone who has old issues earlier than 1950 to lend or donate them to *The Journal* for a reference file. Neither does the Association have a complete set of its *Transactions*. There is one particularly long gap from 1870 to 1888, and some of the other years are not in the best of condition. Any contributions along this line would be very much welcomed.

TELEVISION PROGRAM

Following the plan set up last year, the television program "House Call" has been continued for the past months and has enlisted the assistance of a considerable number of our members who have arranged or appeared on the panels. Columbia, Charleston and Greenville have had regular programs and occasional programs have been presented in Spartanburg and Florence.

The Association is very grateful to those members who have given their time and efforts to carrying out what the Association still believes is a very worthwhile effort to present Medicine to the public in an acceptable and productive form. Since our last report in *The Journal* of April 1960, the following members have participated.

Columbia, Station WIS: Drs. Donald Harwood, John Timmons, Charles Holmes, Benton Montgomery, Ben Miller, Waitus Tanner, Mr. James Daniels, Mr. W. A. Boyce and Mr. D. C. Dick.

Florence, Station WBTW: Drs. Julian Price,

W. R. Mead, J. P. Cain, Jr., W. L. Perry and Prentiss M. Kinney.

Greenville, Station WFBC: Drs. Robert Sumner, H. P. Jackson, A. G. Meakin. W. R. DeLoache, John Juller, Esley Jones, James McNamara, Peter Manos, Earle Furman, William E. Jett, Willis S. Hood, and W. M. Waters.

Charleston, Station WUSN: Drs. Alfred Rawl, Jr., Ely Brooks, F. M. Ball, Otis Pickett, J. J. Cleckley, Joseph Marshall, Junius M. Rowe, Arthur Williams, John Cuttino, T. G. Herbert, Kathleen Riley, Louis Jervey, Robert Walton, Fleetwood Hassell, Margaret Jenkins, Mr. Franklin Robson, Mr. Ray Everett, Mr. G. Searcy, Mr. G. C. Moore.

Present plans, pending final approval by Council, are to continue the television shows to the end of this current year, and then to try to concentrate somewhat more actively on the speakers' activities. A number of scripts have been prepared and have been sent to many areas over the state, and this program which has been started will be continued, on a somewhat larger scale if possible. Some eighteen of our County Societies have indicated a willingness to recruit speakers and to obtain engagements for them before luncheon clubs, civic and community bodies of various sorts, to which they may interpret some of the current problems which concern the doctor and the public. There is still need for further participation in this activity, and the public relations office would be very glad to have replies to the letters sent some time back to all of the County Societies and to have the assurance that the program may be truly statewide.

The television shows which have been presented included the following subjects: Care of the Aged, Food Fadism, Medicine as a Career, Hospital Problems, Poisons in the Home, Hospitalization Insurance, Care and Preservation of the American Business Man, and Mental Health. In addition, other subjects such as a program based on the South Carolina Legislative Committee Report on Problems of the Aging in South Carolina, and How to Reduce your Medical Costs, are in course of preparation.

The scripts which are furnished to the participants are merely suggestions and outlines, and there has been a good deal of necessary variation and addition at the time of actual presentation.

The same applies to the speeches which have been furnished. They are: Food Fadism, Rising Cost of Hospitalization, Care and Preservation of the American Businessman, Hidden Hazards, Poisons, Medicine as a Career, and Mental Health.

COFFEE BREAKFAST AND COFFEE BREAKS

There are those who like to start the day well fortified by a substantial amount of fuel derived from a good breakfast. There are others who gulp a cup of coffee and call it quits. The latter class has always seemed queer to one with a healthy appetite. Perhaps it counts on an early snack in the morning break which seems to be obligatory in most activities.

Studies of work capacity of people who have no breakfast but indulge in the midmorning break, providing miscellaneous food, indicate that the performance of these people is significantly less efficient than that of others who eat a conventional breakfast. Maybe this weakens the argument for the numerous breaks now considered essential by many workers. The time seems to be coming when the breaks will be for work rather than refreshment.

Please pass the ham and eggs.

BENEVOLENCE FUND

BENEVOLENCE FUNDS IN OTHER STATES

Dr. Beverly C. Smith, a distinguished surgeon of New York, has published a brochure covering information obtained by him concerning the establishment of benevolence funds by the various state medical associations and local organizations established for giving pecuniary aid to indigent physicians and their families.

This is titled, "A report on indigency among physicians and how it is handled in each state as reported by the executive secretaries of the societies of the 48 states and District of Columbia. By Beverly Chew Smith, New York City."

Indigency amongst physicians, their wives and widows is known by those administering the affairs of Physicians' Home in New York State to exist in this state to a greater degree than is known by the profession and the public. It is not only increasing, but economical and professional factors, which contribute to indigency, are becoming more active and obvious. Physicians' Home in New York State has currently helped as many as 60 applicants for beneficial aid in one year. We feel there are more than this number in the state whom we do not know of because they do not know of the Physicians' Home or are too proud to expose their indigency. The admission of financial failure seems to be more difficult in this professional group. After two attempts to establish a physical home had proven unpopular with guests, prohibitively expensive and eventually unsuccessful for very fundamental reasons, the idea was abandoned and the policy of sending a monthly stipend to the beneficiary—termed a guest—and allowing him to live where and with whom he chooses, was adopted by the board of directors. This policy has been successfully pursued since 1936. Having been intimately concerned with this problem in New York State for the past twenty years and having been cognizant of its increase, the author felt it might be constructive to know to what degree this situation exists in each of the other states. I, therefore, wrote the executive secretaries of each state medical society and the District of Columbia, asking whether the society recognized this problem, and, if so, what was being done to investigate and remedy it.

The results of this survey showed that there are 16 states that have established funds for this purpose. Thirty-two stated that no provisions had been made and one reported that the Women's Auxiliary provide the care necessary.

In adopting a plan for the establishment of a Benevolence Fund at its May 1960 meeting the South Carolina Medical Association became the 17th state to take this step.

In concluding this report of his study Dr. Smith stated in part as follows:

"On the basis of his experience in New York State, the author cannot in all cases accept the assertion that indigency or near indigency does not exist in states that do not know of it, who have never investigated its existence. Doctors, their wives and widows are so proud that they have been found starving before admitting indigency. However, when financial aid is offered them, it is accepted with a heart-rendering gratitude. The author feels that there exists a state of near financial depletion in a number of instances amongst doctors which could be remedied by a small periodic gift or loan without interest. This study has brought forth violent expressions concerning "Social Security" for the medical profession, but these expressions were obviously made without understanding of the facts of this government agency. Finally, there will always be charity. The usefulness of the latter to obliterate or modify the former will depend upon investigation and wise administration."

BENEVOLENCE FUND

Directors
W. Atmar Smith, M. D.
O. B. Mayer, M. D.
Thomas G. Goldsmith, M. D.

Contributions	
"Survivors", Class of 1910—Medical College of South Carolina	$ 50.00
Temporary Allotment, South Carolina Medical Association	500.00
	$550.00
Distribution to Beneficiaries	250.00
Approximate Balance	$300.00

Beneficiaries — 2 Physicians

BIENNIAL REGISTRATION

Harold E. Jervey, M. D.

There has been discussion since the annual meeting of the State Association concerning the wisdom of supporting legislation for biennial registration of physicians. There are those who maintain that they have heard no reasons presented as to the desirability or need for it. There are others who, while admitting to having heard it discussed, do not feel the arguments offered are sufficiently strong. For the benefit of all groups this brief article has been prepared.

In the fall of 1958, as secretary of the Board of Medical Examiners, I appeared before the Council of the state Association. I discussed all aspects of the proposal, answered the questions posed and requested that they support biennial registration. This they did without a dissenting vote. Later in the year, I appeared before the annual meeting of all county medical officers, discussed the idea and answered questions. A rough draft of the proposal was then presented to the Committee on Public Policy and Legislation. This committee passed it favorably and submitted it to the House of Delegates in May 1959. I appeared before the Reference Committee to which it was submitted, spoke for it, and answered questions. There was no other physician present who showed any

interest in the matter other than the committee. The House of Delegates passed the proposal in principle stipulating that a maximum fee of five dollars be placed in the proposal and requesting that the details be completed and presented for final action in 1960.

This year as you know it was resubmitted and once again was passed. Since 1958, the minutes of several of these meetings have been published in the *Journal of the South Carolina Medical Association*. Also, over this span of time, the individual board members and other interested doctors have discussed the proposal with many others over the state. It would not seem possible that there could be still some who have heard nothing about it or who have unanswered questions if they have made any effort to obtain the answers.

Before presenting specifics, I should like to present some of the considerations which led the board into adopting and actively supporting this legislation. For a number of years, the South Carolina Board had discussed the idea. In my activities with the Federation of State Medical Boards, I discussed the pros and cons with Board members from every state in the union. Subsequently, in my work with the AMA Disciplinary Committee and discussion with state medical society officers from all over the country my convictions were strengthened even more. There was complete unanimity in both groups as to the desirability and necessity for any board to have Registration if they were going to do their job properly and medicine was to police its own ranks. Even among the other Boards of South Carolina this has been found necessary to function properly. All felt that the most progressive legislation that they had enacted was registration and even though many had operated for years without it neither the men representing the state societies nor those representing the Boards could visualize any need for going back. At the beginning of the year, forty-two states had it. In talking to various members this year, at least two others have had it passed and the others are attempting to pass it. Sheer numbers is no argument for it, but the reasons that it has been adopted widely speak strongly for it. No state has adopted it without lengthy debate but once adopted even the opposition has been favorably impressed with the results. This I know, having talked with some of these men.

In presenting it in the manner that the South Carolina Board did, we attempted to avoid some of the errors made by other boards. Also, we have attempted to avoid a public fight and settle the disagreements within the confines of the medical profession. As you may not be aware, the Board of Medical Examiners is a department of state government. As such, it has the right and duty to recommend legislation at any time directly to the legislature which it believes is necessary for the fulfillment of its responsibilities or to protect the people of the state. This course could have been followed with resultant favorable or unfavorable action by the legislature in the session of 1959. However, as this particular legislation affected all physicians and to a nominal extent their pocketbooks, it was felt desirable to clear it through the state association and obtain their support. It was recognized that whereas unanimity was desirable it was far from realistic. Once it had cleared these channels, it was felt that the minority would follow the desires of the majority and a legislative fight and possible adverse newspaper publicity would be avoided. In many states in which this has been recently passed much favorable publicity was accorded the profession for recognizing their responsibilities and willingly supporting regimentation for the betterment of the profession and the public. If sufficient opposition is developed it will undoubtedly be to the detriment of the entire profession. Our disagreements should be kept within our own ranks which is what the Board has attempted to do. Much time and effort has been spent in attempting to familiarize all physicians of the State with the need for this action. This article is another effort in that direction.

There are approximately 140,000 members of the AMA. This represents the majority of physicians that have any contact with organized medicine and can be disciplined or kept in line through medical societies. On the other hand, there are 220,000 licensed physicians practicing medicine in this country. This is a conservative estimate. No accurate figure can be obtained unless all licensing boards have registration and can give an accurate count of those in its state. At any rate, there are 80,000 or more physicians who can only be kept track of and disciplined through the Boards of Medical Examiners. Any licensing board which does not know where its licensees are practicing and if they are practicing has a blind spot and cannot maintain its records or responsibilities to the people of its state or to organized medicine.

In South Carolina, the board has estimated through indirect methods that there are some 2,500 physicians holding licenses and in active practice. Once a license is granted, it remains in effect unless disciplinary action is brought or the individual dies. As a result, the South Carolina Board cannot give you an accurate figure of the number of physicians even practicing within the State of South Carolina. Neither can this be supplied by the Association headquarters. Only a highly intelligent guess can be made. In small areas of the state with a limited number of doctors there is little difficulty keeping up with the number present but in the more heavily populated sections, it is not quite so simple and in addition consideration has to be made for state and governmental agencies. And, as the state becomes more heavily industrialized, plant and union doctors will become a problem.

As a result of not knowing where the licensees are, the South Carolina Board is unable to exercise proper control. A physician may have disciplinary action brought in another state and then move back to South Carolina. This has probably happened on several occasions but it was caught on one occasion in recent years. In a like fashion, if the South Carolina Board disciplines a doctor and he moves out of the State, this information cannot be properly directed unless

there is registration and the Board can know where the physician is located. If all boards have registration, then all physicians can be kept up with, but as long as there are two or three which do not there will be a gap in the mechanism and to some degree will be likened to a fugitive going to another country.

It is not possible for a small state with limited funds and personnel to check on the disciplinary actions taken by all boards. If an alphabetical list of all licenses in effect were available, then it would be relatively simple. All boards have to work together in the area of medical discipline, not only to fulfill their own obligations, but obligation to medicine as a whole. Medical discipline especially in the light of the foreign medical graduate problem, will be brought more and more before the eye of the public. It is essential for the welfare of the profession and the people that they be made to realize that medicine is policing its own ranks and protecting the public from the unethical and disreputable. Registration is an important mechanism in the achievement of this goal.

Even if there were no additional reasons to be offered, the above should be adequate. As mentioned previously, estimates of from 1600 to 1800 physicians have been quoted in articles as practicing in the State of South Carolina. There are many groups who require such figures for papers and surveys being conducted. This encompasses such areas as statistical studies, conclusions on the need for additional medical school facilities based on physician-population ratio, and granting of federal funds for medical purposes rely on accurate figures. In addition, for sociological studies regarding movement of physicians, various scientific papers, and on the broad field of medicine such statistics as to why physicians move and to where are utilized. There are countless numbers of examples that could be given.

To the South Carolina Board, in addition to these, many request for information on licensees from legitimate sources are received. On many occasions information cannot be given because the board does not know the whereabouts of some licensees and does not have the staff to find out. This limits the service that we can perform and also makes it appear at times that we are grossly inefficient. Biennial registration would increase our efficiency in this area. There are many ramifications of the above which could be gone into but the main features as to why this legislation is necessary has been stated above.

Those who oppose this legislation have had only a few points to make. One is to the effect that this is merely a means for the board to raise additional funds. This is not so, but if it were, it would be a valid reason. The South Carolina Board operates on a budget of approximately $7000 a year. At least one and possibly more of the county medical societies in this state have a budget of this amount. Our scope of responsibility and activity far surpasses any county medical society. The South Carolina Board operates on one of the lowest budgets in the country. The highest is the California Board; the State of California appropriates $400,000 plus per year for the operation of its board. At the present time, once a physician has been licensed in this state neither he nor the state government contributes one cent to the operation of the board. It would be highly desirable to have additional funds. Of more importance, the physicians of the state should recognize their responsibility in the proper regulation of medicine and be willing to contribute to the efficiency of operation. The $5.00 every two years that has been stipulated will not contribute any additional operating revenue. It will probably take this to set up the files, conduct the correspondence, procure additional secretarial help, print a booklet listing all licensees and handle other expenses in this regard. It is highly unlikely that funds will evolve. The only reason that a medium of efficiency is maintained is that countless hours of service are rendered with no charge. The men of the board are dedicated to their jobs and the performance of their duties to the profession and to the people of the state. The profession as a whole should recognize their obligation and fulfill their responsibilities as is most fitting. The board only desires that physicians have an understanding of the problems and realize that the board is attempting to do its job in a fashion that will reflect credit on the entire profession.

In conclusion, I should say that the Board of Medical Examiners after much study and discussion does not feel that it can fulfill its responsibilities and operate efficiently without biennial registration.

SCHEDULE OF ACTIVE IMMUNIZATION FOR INFANTS AND CHILDREN

RECOMMENDED BY THE COMMITTEE ON CONTROL OF INFECTIOUS DISEASES OF THE AMERICAN ACADEMY OF PEDIATRICS

AGE	PREPARATION
1½ - 2 months	D.P.T. Poliovaccine
3 months	D.P.T. Poliovaccine
4 months	D.P.T. Poliovaccine
10 - 12 months	Smallpox Vaccine
12 - 18 months	D.P.T. Poliovaccine
3 - 4 years	D.P.T. Poliovaccine
5 - 6 years	Smallpox Vaccine
8 years	D.T. (Adult type) Poliovaccine
12 years	D.T. (Adult type) Poliovaccine
16 years	D.T. (Adult type) Poliovaccine

MEDICAL COLLEGE OFFERS SYMPOSIA TO GROUPS IN THE STATE

The Medical College of South Carolina has been able to provide a modest budget for and is offering through its Continuation Education Program the following symposia:

1. The Present Day Management of Hypertension
   Speakers: Cheves M. Smythe, M. D., Assistant Professor of Medicine.
   Kenneth M. Lynch, Jr., M. D., Professor of Urology.
   W. W. Vallotton, M. D., Associate Professor of Ophthalmology.

2. Strokes.
   Speakers: Vince Moseley, M. D., Professor of Medicine.
   O. Rhett Talbert, M. D., Assistant Professor of Neurology.
   Harry W. Mims, M. D., Associate Professor of Rehabilitation and Physical Medicine.

3. The Menopause.
   Speakers: J. Jennings Cleckley, M. D., Professor of Psychiatry.
   E. J. Dennis, M. D., Assistant Professor of Obstetrics & Gynecology.
   George G. Durst, M. D., Professor of General Practice.

4. The Use and Abuse of Antibiotics.
   Speakers: Louis P. Jervey, M. D., Associate in Medicine.
   Ben H. Boltjes, M. D., Professor of Microbiology.
   Randolph Bradham, M. D., Assistant Professor of Surgery.

5. The Lymphomas.
   Speakers: Charlton de Saussure, M. D., Assistant Professor of Medicine.
   John C. Hawk, M. D., Associate Professor of Surgery.
   Harold S. Pettit, M. D., Clinical Professor of Radiology.

6. What's New in Liver Disease.
   Speakers: Forde A. McIver, M. D., Assistant Professor of Pathology.
   Dan W. Ellis, M. D., Professor of Clinical Pathology.
   Cheves M. Smythe, M. D., Assistant Professor of Medicine.

7. Thyroid Disease — Diagnosis and Treatment.
   Speakers: John E. Buse, M. D., Assistant Professor of Medicine.
   Maria G. Buse, M. D., Instructor in Chemistry.
   R. Randolph Bradham, M. D., Assistant Professor of Surgery.

8. Recent Advances in Coronary Disease:
   Speakers: Dale Groom, M. D., Assistant Professor of Medicine.
   Edwin Boyle, M. D., Associate in Medicine.
   J. M. Stallworth, M. D., Assistant Professor of Surgery.

These are designed as one-night circuit courses for presentation in various areas of the state during the year 1960-61. Each subject is prepared in advance by the three panelists plus a moderator, and presented as a panel discussicn. The programs will be presented without charge. The suggested schedule is a 4:30 to 6:00 p. m. presentation, followed by refreshments, dutch dinner and a period for questions and answers.

The symposia are not primarily intended to provide program material for County medical meetings but rather as a new effort in post-graduate education in South Carolina, the continuation of which will depend upon the demand made for their use. The idea is to have the three or four speakers go to convenient places for local men to attend these with a minimum of loss of time from a busy practice. It is felt that this will encourage attendance by men who have difficulty in attending state wide meetings.

The American Academy of General Practice has approved each of these for three and one-half hours of Category I credit. This effort, if properly used, could therefore assist the membership drive of the Academy by making Category I credit courses more readily available to some potential members who have in the past had difficulty with this requirement.

Persons interested in these offerings should communicate with Dr. Dale Groom, Chairman of the Committee on Continuation Education of the Medical College. Arrangements can then be worked out as to time, place, attendance and program for presentation.

The Committee on Continuation Education wishes to encourage the physicians of the state to use the facilities of the Medical College for study. Special provisions can be made through the Chairman of this committee, Dr. Dale Groom, for any physician desiring to visit any departments or laboratories of the college for special studies or conferences.

News

MEDICAL COLLEGE EXPANSION

An approximately $100,000 expansion project at the out-patient clinic of the Medical College Hospital has begun.

College officials awarded a contract for the work to Palmetto Construction Co. of Charleston.

A second stage of the out-patient clinic expansion program will include the ground floor of a million-dollar research building. The research center is still being designed but is expected to be in operation in about two years.

Other expansion plans at the South Carolina medical training and treatment center here include the psychiatric department. This program is estimated to cost about $500,000.

The expansion is being financed with funds from the Hill-Burton federal program and college tuition revenue bonds.

S. C. A. G. P. NAMES NEW OFFICERS

The South Carolina Academy of General Practice named new officers at the annual meeting held in September. They are Dr. Jim Blanton of Chesnee, treasurer; Dr. Swift Black of Dillon, president-elect; Dr. Martin M. Teague of Laurens, president; Dr. Horace Whitworth of Greenville, vice president; and Dr. Bill Bannon of Simpsonville, secretary.

RURAL HEALTH CONFERENCE HEARS DR. PRICE

Dr. Julian P. Price, chairman of the board of trustees of the American Medical Association was among the speakers at the first regional conference on Rural Health in Atlanta October 7-8.

"Joining Hands for Community Health" was the theme of the 11-state meeting sponsored by AMA's Council on Rural Health.

The Annual Meeting of the South Carolina Orthopedic Association was held at the William Hilton Hotel at Hilton Head, South Carolina, September 16, 17, 18, 1960. The program included papers by Drs. David Holler, Thomas Edwards, David Riddle, Ritchie Belser, Hiram Kite, Emmett M. Lunceford, Frank Stelling, Austin Moore, Francis Gay, James T. Green, and G. M. Gudmundson. Dr. William Boyd of Columbia was presented with a testimonial plaque indicating appreciation for his long membership and vital interest in orthopedics in South Carolina. Dr. Hiram Kite of Atlanta was guest speaker and was elected to honorary membership. Officers elected were: President, Dr. John A. Siegling of Charleston, Vice president, Dr. Frank Stelling of Greenville; and Secretary-Treasurer, Dr. James Green of Columbia. Dr. William Boyd of Columbia was elected President emeritus.

AMERICAN MEDICAL EDUCATION FOUNDATION

As a product of The South Carolina Plan the July 1960 issue of *The Foundation News* carries the following items.

Of the sixteen (16) awards of merit for 1959 to individuals for outstanding contributions to their medical schools through the A. M. E. F., eight (8) are to members of the faculty of the Medical College of South Carolina. They are Dr. Ben H. Boltjes, Professor of Microbiology, Dr. J. J. Cleckley, Professor of Psychiatry, Dr. Daniel W. Ellis, Professor of Clinical Pathology, Dr. Robert F. Hagerty, Associate Professor of Surgery, Dr. John E. Mahaffey, Assistant Professor of Anesthesiology, Dr. John H. Murdoch, Jr., Assistant Professor of Clinical Pathology, Dr. Harold S. Pettit, Professor of Radiology, and Dr. H. Rawling Pratt-Thomas, Professor of Pathology.

Also, listed as receiving the new A. M. E. F. *Citation*, awarded for the first time, are two other members of the faculty, Dr. Kenneth M. Lynch, now Chancellor and Dr. Vince Moseley, now Dean of Clinical Medicine and Professor of Medicine.

Among the organizations given *Awards of Merit* for 1959 is the Medical College of South Carolina Alumni Association.

J. Howard Stokes, M. D., Chairman, Florence
R. L. Crawford, M. D., Lancaster
Thomas R. Gaines, M. D., Anderson
Medical Education Foundation Committee
South Carolina Medical Association

AUGUST SCIENTIFIC MEETING OF THE COLUMBIA MEDICAL SOCIETY

The medical staff of the South Carolina State Hospital was host to the Columbia Medical Society for the Scientific Meeting on August 8, 1960. Dinner was served in the Benet Auditorium prior to the Scientific Program.

Dr. W. A. Hart, President of the Columbia Medical Society, presented Dr. William S. Hall, Superintendent of the South Carolina State Hospital, who spoke on "The Mental Health Act and the Private Practicing Physician".

With the aid of slides, Dr. Hall explained the new South Carolina Mental Health Act of 1952, which closely resembles the model Mental Health Act drafted by the National Institute for Mental Health.

He explained the five types of admission procedures and the necessity for physicians in private practice to understand each and the responsibility involved in the admission of a patient to a mental hospital.

The new Mental Health Act safeguards the rights of the patients; and represents a definite advance in the mental health field in South Carolina, Dr. Hall

explained. One important phase of the new act is the deletion of objectionable terms, and especially the substitution of the term "mentally ill."

Dr. Hall stressed the objectives of the South Carolina State Hospital and the responsibility resting upon the hospital to provide the best possible care for the mentally ill with maximum opportunities for prompt medical and mental care. The various ways for a patient to be separated from the hospital were explained. Dr. Hall also went into the new interstate compact which permits treatment of a mentally ill person in the indicated state on the basis of mental need and desired close proximity to family rather than enforced care in the state of residence.

TRIBUTE PAID TO DR. P. K. SWITZER, SR.

At a recent meeting held jointly by the Union County Medical Society and the Union Nurses Club, tribute was paid to Dr. Paul Kent Switzer, Sr., in recognition of his Golden Anniversary as a physician.

Dr. Harold P. Hope presented Dr. Switzer with an engraved silver cigarette chest on behalf of the Medical Society, and in words of appreciation attributed much of the success of the Society to the leadership, cooperation and wonderful example set by Dr. Switzer in his 50 years as a doctor. Gifts were also presented to Dr. Switzer by Dr. Francis P. Owings on behalf of the American Medical Association and Mrs. W. C. Bennett, president of the Nurses Club. Dr. Boyd L. Hames was Toastmaster for the occasion. Dr. Joseph H. Guess rendered the invocation.

Dr. Switzer was born in Switzer, S. C. in 1885 and graduated from the Medical College of the State of S. C. in 1910. After four years of practice in Fort Motte, S. C., he began his practice in Union in 1914.

Among the out-of-town Associate Members of the Union County Medical Society who attended the meeting were Drs. Charlton P. Armstrong, Jr. of Greenville; William A. Matthews of Rock Hill; Leslie C. Meyer of Greenville, William B. Ward of Rock Hill; and Theodore S. Wedde of Rock Hill.

DOCTOR WALKER OPENS OFFICE

Dr. Thurmond O. Walker has announced the opening of his office for the general practice of medicine at 1207 Sunset Blvd., West Columbia, in association with Dr. Richard W. Thomas.

Dr. Walker attended Columbia City schools and received a B.S. degree from the University of South Carolina in 1954. He graduated from the Medical College of South Carolina in 1958.

He did his rotating internship at the Columbia Hospital in 1958 and 1959. Since completing this he has been associated with the South Carolina State Hospital as staff physician.

DR. BRADFORD JOINS STAFF OF STATE HOSPITAL

Dr. Reese W. Bradford has assumed his position on the medical staff of the South Carolina State Hospital with assignment to the men's service, Columbia Unit, as announced by the hospital superintendent, Dr. William S. Hall.

"But, Doctor, I'm supposed to say 'A'!"

A native of Georgia, Dr. Bradford attended the University of Georgia at Athens, and received his medical degree from the Medical College of Georgia, Augusta.

He recently retired as assistant superintendent of the Milledgeville State Hospital, Milledgeville, Ga., where he had been during his entire professional career.

SURGEON TO JOIN HOSPITAL

Beaufort Memorial Hospital next month will gain a staff surgeon when Dr. R. L. Redfield assumes his duties at the county medical center.

A native of Pleasantville, Pa., Dr. Redfield settled in Oil City shortly before World War II and pursued a successful medical career in that city until his move to Beaufort.

Well known in Pennsylvania medical circles, Dr. Redfield had been a member of the Oil City Hospital surgical staff since 1941 and its chief for many years. He is a member of the American College of Surgeons and the International College of Surgeons.

He is a graduate of Jefferson Medical College, Philadelphia, and interned at St. Vincent Hospital in Erie, Pa., before completing his surgical residency at the Millard Fillmore Hospital in Buffalo, N. Y.

DR. ROSENBERG IS PRESIDENT PIEDMONT CLINICAL GROUP

Abbeville's Dr. George V. Rosenberg is the new president of the Piedmont Post Graduate Clinical Assembly, succeeding Dr. John T. Davis of Walhalla.

Dr. Rosenberg was named to the post at the recent 25th annual meeting at the Clemson House, which included a two-day series of lectures, discussions and banquets.

Other officers chosen were Dr. William Lummus,

Anderson, executive vice president; Dr. Frank Espey, Greenville, and Dr. Lewis Cacchiola, Hartwell, Ga., vice presidents; Dr. William H. Hunter, Clemson, registrar, and Dr. Ned Camp, Anderson, secretary-treasurer.

A native of Abbeville, Dr. Rosenberg graduated from Abbeville High School and The Citadel. He won his M. D. degree from the Medical College of South Carolina and interned at Roper Hospital, Charleston. He has served as president of the Abbeville County Medical Society and the Third District Medical Society, and is on the staffs of Abbeville County Memorial and Self Memorial Hospitals.

MULTIPLE SCLEROSIS MEETING

A statewide meeting to reorganize the South Carolina Multiple Sclerosis Society was held in Columbia on September 11.

Dr. W. H. Bridgers of Columbia spoke about the disease and its treatment. Dr. Rhett Talbert of the Charleston Medical College discussed research in the MS field. Emmett Carraher, regional director of the national society told of the need for volunteer workers.

Dr. Hugh W. Mole of Denmark is now registered and is a member of The American Board of Abdominal Surgery. Dr. Mole is a regular staff member of Bamberg County Memorial Hospital. He also practices in Orangeburg and Barnwell hospitals.

DR. DICKSON OPENS OFFICE

Dr. Griggs C. Dickson has opened an office for the practice of pediatric medicine in Hartsville. Offices are located at 807 Carolina Avenue, where he will be joined in November by Dr. James C. Parke, Jr., now completing a term of service as staff pediatrician at U. S. Naval Hospital, Portsmouth, Va.

Dr. Dickson is a native of Garner, N. C. He graduated from the University of North Carolina with the degree of B. S. in Medicine. In 1955 he received his M. D. degree from the University of North Carolina School of Medicine.

He served his internship at North Carolina Memorial Hospital in Chapel Hill in 1955-56 and his residency in pediatrics there in 1956-57. He was in the U. S. Navy during the period 1957-59, serving with the pediatric department of U. S. Naval Hospital at Portsmouth, Va.

From 1959 until the present, Dr. Dickson has been chief resident and instructor in the Department of Pediatrics at North Carolina Memorial Hospital.

The Seventh District Medical Association held a meeting at Kingstree on September 22, 1960. Speakers were Drs. John F. Buse, Jr., J. Manly Stallworth, H. R. Pratt-Thomas, and Clarence W. Legerton, all of Charleston.

The Coastal Medical Society held its meeting on September 22nd at Walterboro.

Announcements

ANNOUNCEMENT FOR GENERAL PRACTITIONERS AND INTERNISTS

Applications for Charter Membership in the American Society of Diagnostic Radiology are now being received. Membership is open to General Practitioners and Internists *who do or may desire to do some types of Diagnostic Radiology in their offices.*

For further information please write

Louis Shattuck Baer, M. D., F. A. C. P.
411 Primrose Road
Burlingame, Calif.

MEDICAL COLLEGE OF GEORGIA AND FOUNDATION PRESENT PROBLEMS OF THE NEWBORN INFANT

January 24, 25, 26, 1961

Registration is limited to a small group for close participant-faculty communication. Application form should be filled out and mailed, together with the fee, as soon as possible. Registration will be officially confirmed.

A block of rooms has been reserved at the Medical Center Motel on Gwinnett Street across from Talmadge Hospital. Reservation cards will be sent direct to the registrants with a letter confirming acceptance to the course. Meals will be available in the immediate area.

Each course is acceptable for 18 hours credit, Category I, by the American Academy of General Practice.

A symposium on Clinical Nutrition will be held in Washington, D. C. on November 30, 1960. This symposium, sponsored by the Council on Foods and Nutrition of the American Medical Association in cooperation with The Medical Society of the District of Columbia, will begin at 8:30 a. m. Wednesday, November 30, in Room B of the National Guard Armory. The meeting will be opened to all interested persons.

There is a definite need for a general practitioner to locate in St. Stephen, South Carolina.

Since the death of Dr. T. B. Harper in that town, and the death of two physicians in surrounding communities, the patient load on the one general practitioner is entirely too heavy.

AMERICAN COLLEGE OF SURGEONS

Members of the medical profession are invited to attend an instructive three-day Sectional Meeting of the American College of Surgeons being held in Birmingham, Alabama, January 16, 17, 18, 1961. Headquarters hotel for the meeting will be the Dinkler-Tutwiler.

The Columbia Medical Society will hold its Annual Meeting for the Election of Officers at the Hotel Columbia, Columbia, S. C., Monday, December 12, 1960, at 8:30 P. M.

ANNUAL REPORT OF THE CRIPPLED CHILDREN SOCIETY OF SOUTH CAROLINA, INC.

The Chairman of the Medical Advisory Committee to the Society has received a full report and wishes to pick out the more important and interesting points which it contains.

The Report begins with a brief history of the Society, now 25 years old and developing annually into greater activities. The chief objective of the Society is "To engage in activities to improve the health, welfare, education, rehabilitation, employment, recreation, facilities and opportunities of crippled children and adults of the State, regardless of race, color or creed." Twelve years ago the Society secured the assistance of the National Society of which it is a Chapter for professional guidance in making a state-wide survey in South Carolina in order to determine needs and to develop plans. Following this survey, it was decided that the efforts of the Society be concentrated on a state-wide cerebral palsy program which was to include not only actual service to patients but public educational activities, parent education, professional education and cooperation with other agencies concerned with the field of the crippled child. This program has included case findings, diagnostic and evaluation clinics, treatment centers, special committees to work with legislators and arrangements to work with the Vocational Rehabilitation Department. The survey showed that there would be an estimated 2,600 cerebral palsied children under the age of 21 in the state with 1,110 of this number in need of special services. The program has expanded to include a very large part of these potential patients and it is subjected to review periodically in order to bring it up to date.

Educational activities have been carried out through the press, radio, television, speakers' reports and miscellaneous literature. Conferences with parents are held very frequently and efforts toward improving the activities of professional workers have been unceasing.

The Society has interested itself in promoting special education of teachers who might handle special classes in the school and work with cerebral palsied and other handicapped children. Effective legislation to promote this activity may be traced very largely to the efforts of the Crippled Children Society and particularly of its efficient Executive Director, Mrs. Lowe.

The Society has also underwritten expenses of a speaker at the recent annual meetings of the South Carolina Medical Association in order to keep the problem of cerebral palsy and its solution before the medical profession.

At the present the Society has a total of 440 cerebral palsied children and 38 adults on its active rolls for care in South Carolina. An additional 222 cases have been seen in the Easter Seal Clinics and been referred to other agencies whose facilities are more appropriate for their care. County Chapters have also provided funds to State tax-supported agencies to supplement services available to 586 cerebral palsied. The number here, added to the number on the active rolls of the Society would bring the total number of cases assisted by Easter Seal funds in South Carolina to 1,398. A State Easter Seal Cerebral Palsy Diagnostic and Evaluation Center with full staff is operated in Columbia. Greenville County has utilized its Easter Seal funds for setting up a Sheltered Workshop program. Other Easter Seal Centers are located in Charleston, Aiken, Greenwood, Rock Hill, and Spartanburg.

The Third Annual Easter Seal Family Camp was held in 1960. This provides camping activities for children who are too much handicapped to attend other camps and the opportunity for many counseling sessions with parents and various consultants.

Believing that basic research in the problem of cerebral palsy is essential to the progress of its program, the Society has given grants over the past several years to Dr. Isabel Lockard of the Medical College of South Carolina.

Believing also that there is a special necessity for training teachers in the conduct of special education for the handicapped child, the Society has made a grant of $9,000 a year for a three-year period to the University of South Carolina for the establishment of a Chair of Special Education.

The financial report is impressive. The total amount spent for the fiscal year from the Easter Seal Campaign and special donations amounted to $210,076.00. Incidentally, in the past two years the Easter Seal Funds have been expended for direct care and treatment services benefitting handicapped South Carolinians to the extent of $419,596.00. In the five-year period past, almost $125,000.00 has been expended for special education services for children with cerebral palsy and other crippling and handicapping conditions.

These brief remarks do not include all of the interesting and important material which is carried in the Annual Report of the Society. Many details and some

activities have been omitted. It is suggested that those who are interested in having the full story might write for a copy of the full report to Mrs. T. Jackson Lowe, 1517 Laurel Street, Columbia, S. C.

J. I. Waring, Chairman

Book Reviews

DISEASES OF THE NEWBORN, by Alexander J. Schaffer, M. D. With a Section on Neonatal Cardiology by Milton Markowitz, M. D. W. B. Saunders Company: Philadelphia, 1960. Price $20.00.

This is a large volume of more than eight hundred pages which covers in considerable detail the subject of diseases in the newborn. Except for the one section on neonatal cardiology by Markowitz, the book is entirely the work of the author, and is not a compilation or an edited collection. The subjects are well covered, and the exposition is well expressed. The author offers many case reports which are pertinent to the subjects under discussion, and many illustrations which point up the special matters in question.

The author is not categorical in his pronouncements, and frequently expresses a feeling that the subject under discussion is not a closed one and that his own view may not be entirely the correct one. Ample room for argument is left to the reader.

If after seeing this very worthwhile work, the reader should feel inclined to expand its ample size, it would of necessity be either repetitious or redundant. This book can be recommended without hesitation to anyone interested in that neonatal period which Dr. Schaffer calls the "last frontier of medicine."

JIW

FUNDAMENTALS OF CLINICAL HEMATOLOGY. By Byrd S. Leavell, M. D. and Oscar A. Thorup, M. D. 503 pages. W. B. Saunders Company, Philadelphia. 1960. Price $10.00.

The need for a new text in hematology in view of the number already in existence is open to some question unless it fills a specific purpose or adds something heretofore not available. The authors of this book have attempted, therefore, to present the subject in a concise, brief, overall manner directed primarily to the third year student or busy general practitioner. Consequently a great deal of information is covered in a short space which allows only a cursory review of any particular topic.

The basic format is similar to other texts, starting with a review of the morphology, maturation, and metabolism of the blood cells. This is followed by a short survey of 1) various types of anemias, 2) blood coagulation, 3) diseases of the white cells, and 4) a final chapter of hematological techniques. Brief case reports are presented to illustrate the various syndromes which unfortunately cannot show the protean manifestations of any of the disease states described and do not appear to add much to the overall value.

This book does have the advantage that it is up to date on many of the newer concepts in hematology such as the pathogenesis of various anemias, diagnostic techniques, and more recent modalities of therapy which are not included in older texts. It would seem to fill a limited need as a complete outline for students beginning clinical medicine and allowing them to get a general perspective. For a practitioner interested in a particular phase of hematology, however, it would appear to be too sketchy.

Charlton deSaussure, M. D.

REVIEW OF MEDICAL MICROBIOLOGY, by E. Jawetz, J. L. Melrick, and E. A. Adelberg. 4th Edition. Lange Medical Publications, Los Altos. 1960. pp. 377. Price $5.00.

The authors' intention to write a book for the medical student and the practicing physician has been duly performed. The material of this Review is up to date and presented in a very clear cut and precise form. Anyone seeking information here should find it easily. The material in each chapter is presented in concise outline, which along with the clarity of the authors' writing, makes this an outstanding review.

It would seem to this reviewer that the allocation of only one chapter to the study of mycology is a grave injustice which should have been corrected before this 4th edition was published.

The bacterial and viral diseases are covered adequately. There is enough background material in the book for a good understanding of the principles or techniques involved. This review, as is true in all, suffers from the necessary omissions that are made. The omission of many important descriptions of colonial morphology on various cultural media is one of the reasons this book would not make a text for general microbiology as the authors have suggested.

J. Heyward Wynn, Jr.

RUDOLPH MATAS by Isadore Cohn, M. D. with Hermann B. Deutsch. Doubleday & Company, Inc., Garden City, N. Y., 1960. Price $5.95.

Rudolph Matas, famous surgeon of New Orleans, died only a few years ago at the age of 97. At 80 years he was still performing surgery and his brilliant mind remained active until just immediately before his death.

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Research in the Service of Medicine

Born of a Spanish family, Dr. Matas was raised and educated in New Orleans, where he showed very early in life the evidences of the active part which he would play in Louisiana and world medicine. Before his graduation in medicine he served as an assistant to the commission under Dr. Sternberg and Dr. Chaillé which was sent to Cuba to try to determine the cause of yellow fever. Although the expedition was unsuccessful, the work done by Dr. Finlay on the transmission of the disease by the mosquito was to become the foundation of the final proof of the method of transmission. Dr. Finlay's announcement came out about two years after the commission had failed to find anything definite, and through an intimacy between Matas and Finlay, the former became the permanent champion of the real discoverer of the mosquito vector, and was to translate Finlay's first paper on the subject for publication in a *New Orleans Medical and Surgical Journal.*

Matas made enviable records in his medical school career and at the early age of 21 he became part owner and associate editor of the *New Orleans Medical and Surgical Journal,* at the same time building practice rapidly so that in time he became the foremost physician of New Orleans. There were intervals during which he deserted his practice to serve as yellow fever inspector at Vicksburg and to participate actively in a number of efforts.

Matas was in intimate friend of Lafcadio Hearn and they were inseparable companions for a time.

Matas soon became Demonstrator in Anatomy at Tulane and developed original views on the process in appendicitis. He likewise devised techniques for operation on aneurysm and might be considered as the father of blood vascular surgery. He was active in establishing the New Orleans Polyclinic (postgraduate school) and received world-wide recognition for his many contributions to surgical philosophy and technique; eventually he became Professor of Surgery at Tulane. In 1906 he lost one eye and from that time on he became the surgical artist rather than the originator of surgical manouvers. Honors came to him from many quarters. He was recognized abroad and attended many Congresses and received honorary degrees and awards in some number.

This book gives a review of medicine in New Orleans over a period of almost a century and paints an absorbing picture of the character and achievements of Dr. Matas. This reviewer found it most interesting, well written, and informative. There are parts of the book in which the subject seems to leave the stage almost entirely, and if any fault may be found it is in the touch of the same prolixity which the authors concede was a minor fault of Dr. Matas.

There are one or two oddments which were not quite explicable, such as the photograph of Dr. Matas' stillborn child, which seemed rather superfluous. The use of the term "Bronze John" for yellow fever was not familiar to the reviewer and he wondered whether this was a fancier term for the more familiar "Yellow Jack," or whether Yellow Jack was actually a lineal descendant of Bronze John.

This book should furnish an ample amount of entertainment and instruction to any reader.

JIW

HELP BRINGERS: VERSATILE PHYSICIANS OF NEW JERSEY, by Fred B. Rogers, M. D. Vantage Press, New York, 1960. Price $2.95.

Dr. Rogers, Archivist of the Medical Society of New Jersey, has given us a book which contains a dozen sketches of prominent physicians of the state. Some of these vignettes have already appeared in the *Journal of the Medical Society of New Jersey,* others have been added to complete the lively and entertaining account. The subjects of the sketches cover the period from the very early days until practically the present moment and present a striking variety of characteristics. Of the older group, perhaps Nicholas Belleville was the most colorful, a Frenchman who had close contact with Count Pulaski, Joseph Bonaparte, Lafayette and the prominent physicians of the day of Philadelphia. Dr. Israel Clarke was best known as a wit, Dr. Abraham Coles as a poet and scholar, Dr. Newell for his activities in politics, Dr. English for his surviving poem "Ben Bolt", and others for their multitudinous activities in fields other than medicine. They are impressive because of their many interests, their many activities, and their contributions to the formation of the solid backbone of the medical profession of New Jersey.

The last three doctors represent medical contributions perhaps more realistically. Dr. Ezra Houck was a leader in public health, Dr. Cyrus Fogg Brackett was primarily a physicist and also a practitioner at times; his contributions in physics were recognized as most outstanding. Dr. Henry Leber Coit was a pioneer pediatrician who was firm in his advocacy of public health measures and effective in his effort to secure a proper milk supply. Certified milk was his chief and successful objective.

The articles included in this small book are well written, well presented and engaging in their quality. It is not necessary that one be a citizen of New Jersey to find entertainment and information in their pages.

JIW

With an end in view. Sinai Hosp. J. 9:43-44, Spring 1960. Leon Banov, Jr. (Charleston)

Perhaps the most fundamental handicap in spreading knowledge of anorectal diseases has come about through a difficulty of language. Words often possess ambiguity of meaning. It is suggested that physicians who examine and treat the anorectum should strive to convey the precise meaning of what they wish to describe. By using correct and proper terminology, plus photography, the pace of progress, wherein diseases of the anorectum are concerned, will be accelerated. This is an end in view.